68992

Access DB# _____

Point of C ntact:
Thomas G. Larson, Ph.D.
703-308-7309
CM1, Rm. 6 B 01

SEARCH REQUEST FORM

Scientific and Technical Inf rmation Center

Requester's Full Name: GAOQUN LI Examiner #: 78206 Date: 06/17/2004
Art Unit: 1648 Phone Number 30 5-1695 Serial Number: 09/829,031
Mail Box and Bldg/Room Location: CM1. 8E12 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Reversal of viral-induced systematic shock and respiratory distress by blockage of the lymphotoxin beta p.

Inventors (please provide full names): Browning, Jeffrey. Pulelli, Marianne, Ahmed Ka

Earliest Priority Filing Date: _____

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

please search claim 1-8. directed to the method for inducing an anti-viral response by using an agonist, including an antibody or fusion protein of lymphotoxin-B receptor.

Thanks

Point of Contact:
Thomas G. Larson, Ph.D.
703-308-7309
CM1, Rm. 6 B 01

****

STAFF USE ONLY		Type of Search		Vendors and cost where applicable	
Searcher:	Larson	NA Sequence (#)		STN	730
Searcher Phone #:	8-7309	AA Sequence (#)		Dialog	
Searcher Location:	6B01	Structure (#)		Questel/Orbit	
Date Searcher Picked Up:	6/18	Bibliographic	X	Dr.Link	
Date Completed:	6/24	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:	30	Fulltext		Sequence Systems	
Clerical Prep Time:		Patent Family		WWW/Internet	
Online Time:	302	Other		Other (specify)	

PTO-1590 (8-01)

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=> file medline

FILE 'MEDLINE' ENTERED AT 17:28:27 ON 24 JUN 2002

 FILE LAST UPDATED: 23 JUN 2002 (20020623/UP). FILE COVERS 1958 TO DATE.

 On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> d que L18
L1           362 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L10         9229 SEA FILE=MEDLINE ABB=ON  PLU=ON  RECEPTORS, TUMOR NECROSIS
                 FACTOR+PFT/CT
L12           93 SEA FILE=MEDLINE ABB=ON  PLU=ON  L10 (L) AI/CT
L14            6 SEA FILE=MEDLINE ABB=ON  PLU=ON  L1 AND L12
L15       518045 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTIBODIES+NT,PFT/CT
L16            3 SEA FILE=MEDLINE ABB=ON  PLU=ON  L14 AND L15
L17       108001 SEA FILE=MEDLINE ABB=ON  PLU=ON  SIGNAL TRANSDUCTION+NT,PFT/CT

L18            2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L16 AND L17


=> d que L26
L1           362 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L3          1876 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN+PFT/CT
L10         9229 SEA FILE=MEDLINE ABB=ON  PLU=ON  RECEPTORS, TUMOR NECROSIS
                 FACTOR+PFT/CT
L23          501 SEA FILE=MEDLINE ABB=ON  PLU=ON  L3 (L) (CH. OR TH. OR PD.)/CT

L24          582 SEA FILE=MEDLINE ABB=ON  PLU=ON  L10 (L) (CH. OR TH. OR
                 PD.)/CT
L25           10 SEA FILE=MEDLINE ABB=ON  PLU=ON  L23 AND L24
L26            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L25 AND L1



=> d que L33
L1           362 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L3          1876 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN+PFT/CT
L10         9229 SEA FILE=MEDLINE ABB=ON  PLU=ON  RECEPTORS, TUMOR NECROSIS
                 FACTOR+PFT/CT
L23          501 SEA FILE=MEDLINE ABB=ON  PLU=ON  L3 (L) (CH. OR TH. OR PD.)/CT

L24          582 SEA FILE=MEDLINE ABB=ON  PLU=ON  L10 (L) (CH. OR TH. OR
                 PD.)/CT
L27         1073 SEA FILE=MEDLINE ABB=ON  PLU=ON  L23 OR L24
L28          448 SEA FILE=MEDLINE ABB=ON  PLU=ON  L27/MAJ
L29           25 SEA FILE=MEDLINE ABB=ON  PLU=ON  L28 AND L1
L32       154156 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTIVIRAL AGENTS+NT,PFT/CT
L33            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L29 AND L32
```

AI antagonist & inhibitors subheading

CH-Chemistry subheadings
TH-Therapeutic subheadings
PD-Pharmacological subheadings

→ major focus of document

```
=> d que L41
L1          362 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L3         1876 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN+PFT/CT
L8         9176 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTILYMPHOCYTE SERUM+PFT/CT
L10        9229 SEA FILE=MEDLINE ABB=ON  PLU=ON  RECEPTORS, TUMOR NECROSIS
                FACTOR+PFT/CT
L23         501 SEA FILE=MEDLINE ABB=ON  PLU=ON  L3 (L) (CH. OR TH. OR PD.)/CT

L24         582 SEA FILE=MEDLINE ABB=ON  PLU=ON  L10 (L) (CH. OR TH. OR
                PD.)/CT
L27        1073 SEA FILE=MEDLINE ABB=ON  PLU=ON  L23 OR L24
L36           9 SEA FILE=MEDLINE ABB=ON  PLU=ON  L27 AND L8
L37         527 SEA FILE=MEDLINE ABB=ON  PLU=ON  L3 (L) (TU. OR TH. OR PD. OR
                CH.)/CT
L38         805 SEA FILE=MEDLINE ABB=ON  PLU=ON  L10 (L) (TU. OR TH. OR PD. OR
                CH.)/CT
L39        1321 SEA FILE=MEDLINE ABB=ON  PLU=ON  L37 OR L38
L40           9 SEA FILE=MEDLINE ABB=ON  PLU=ON  L39 AND L36
L41           0 SEA FILE=MEDLINE ABB=ON  PLU=ON  L40 AND L1


=> d que L44
L1          362 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L3         1876 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN+PFT/CT
L10        9229 SEA FILE=MEDLINE ABB=ON  PLU=ON  RECEPTORS, TUMOR NECROSIS
                FACTOR+PFT/CT
L15      518045 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTIBODIES+NT,PFT/CT
L37         527 SEA FILE=MEDLINE ABB=ON  PLU=ON  L3 (L) (TU. OR TH. OR PD. OR
                CH.)/CT
L38         805 SEA FILE=MEDLINE ABB=ON  PLU=ON  L10 (L) (TU. OR TH. OR PD. OR
                CH.)/CT
L39        1321 SEA FILE=MEDLINE ABB=ON  PLU=ON  L37 OR L38
L42         458 SEA FILE=MEDLINE ABB=ON  PLU=ON  L39 AND L15
L43          15 SEA FILE=MEDLINE ABB=ON  PLU=ON  L42 AND L1
L44           3 SEA FILE=MEDLINE ABB=ON  PLU=ON  L43 AND (VIRUS OR VIRAL?)


=> d que L47
L1          362 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L2          112 SEA FILE=MEDLINE ABB=ON  PLU=ON  L1 (3A) RECEPTOR
L3         1876 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN+PFT/CT
L10        9229 SEA FILE=MEDLINE ABB=ON  PLU=ON  RECEPTORS, TUMOR NECROSIS
                FACTOR+PFT/CT
L37         527 SEA FILE=MEDLINE ABB=ON  PLU=ON  L3 (L) (TU. OR TH. OR PD. OR
                CH.)/CT
L38         805 SEA FILE=MEDLINE ABB=ON  PLU=ON  L10 (L) (TU. OR TH. OR PD. OR
                CH.)/CT
L39        1321 SEA FILE=MEDLINE ABB=ON  PLU=ON  L37 OR L38
L45         117 SEA FILE=MEDLINE ABB=ON  PLU=ON  L2 OR (LYMPHOTOXIN BETA-SPECIF
                IC RECEPTOR OR LT.BETA.R OR LT-.BETA.R OR LT-.BETA-R)
L46          12 SEA FILE=MEDLINE ABB=ON  PLU=ON  L45 (5A) (ANTI OR ANTIBOD? OR
                IMMUNOGLOB? OR SOLUBL? OR BLOCK?)
L47           5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L39 AND L46


=> d que L50
L1          362 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L2          112 SEA FILE=MEDLINE ABB=ON  PLU=ON  L1 (3A) RECEPTOR
L3         1876 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN+PFT/CT
L10        9229 SEA FILE=MEDLINE ABB=ON  PLU=ON  RECEPTORS, TUMOR NECROSIS
```

TU therapeutic use subheading

```
                FACTOR+PFT/CT
L37          527 SEA FILE=MEDLINE ABB=ON  PLU=ON  L3 (L) (TU. OR TH. OR PD. OR
                CH.)/CT
L38          805 SEA FILE=MEDLINE ABB=ON  PLU=ON  L10 (L) (TU. OR TH. OR PD. OR
                CH.)/CT
L39         1321 SEA FILE=MEDLINE ABB=ON  PLU=ON  L37 OR L38
L45          117 SEA FILE=MEDLINE ABB=ON  PLU=ON  L2 OR (LYMPHOTOXIN BETA-SPECIF
                IC RECEPTOR OR LT.BETA.R OR LT-.BETA.R OR LT-.BETA-R)
L49            5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L45 (3A) (IG? OR IMMUNOGLOB?)
                (3A) (FUSION (W) (PROTEIN OR PEPTIDE))
L50            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L39 AND L49


=> d que L65
L1           362 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L3          1876 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN+PFT/CT
L10         9229 SEA FILE=MEDLINE ABB=ON  PLU=ON  RECEPTORS, TUMOR NECROSIS
                FACTOR+PFT/CT
L37          527 SEA FILE=MEDLINE ABB=ON  PLU=ON  L3 (L) (TU. OR TH. OR PD. OR
                CH.)/CT
L38          805 SEA FILE=MEDLINE ABB=ON  PLU=ON  L10 (L) (TU. OR TH. OR PD. OR
                CH.)/CT
L39         1321 SEA FILE=MEDLINE ABB=ON  PLU=ON  L37 OR L38
L56       128791 SEA FILE=MEDLINE ABB=ON  PLU=ON  DNA VIRUSES+NT,PFT/CT
L57       188948 SEA FILE=MEDLINE ABB=ON  PLU=ON  RNA VIRUSES+NT,PFT/CT
L58       307991 SEA FILE=MEDLINE ABB=ON  PLU=ON  VERTEBRATE VIRUSES+NT,PFT/CT
L59       307991 SEA FILE=MEDLINE ABB=ON  PLU=ON  L56 OR L57 OR L58
L63          616 SEA FILE=MEDLINE ABB=ON  PLU=ON  L39/MAJ
L64           30 SEA FILE=MEDLINE ABB=ON  PLU=ON  L63 AND L59
L65            4 SEA FILE=MEDLINE ABB=ON  PLU=ON  L64 AND L1


=> s l18 or l26 or l33 or l44 or l47 or l50 or l65
L174          10 L18 OR L26 OR L33 OR L44 OR L47 OR L50 OR L65

=> file embase
FILE 'EMBASE' ENTERED AT 17:32:36 ON 24 JUN 2002
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 FILE COVERS 1974 TO 20 Jun 2002 (20020620/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que L79
L67         2232 SEA FILE=EMBASE ABB=ON  PLU=ON  LYMPHOTOXIN+PFT/CT
L68         3301 SEA FILE=EMBASE ABB=ON  PLU=ON  TUMOR NECROSIS FACTOR RECEPTOR+
                PFT/CT
L69         5389 SEA FILE=EMBASE ABB=ON  PLU=ON  L67 OR L68
L70          301 SEA FILE=EMBASE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L72       281191 SEA FILE=EMBASE ABB=ON  PLU=ON  VIRUS+PFT/CT OR DNA VIRUS+NT,PF
                T/CT OR RNA VIRUS+NT,PFT/CT
L76       345967 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTIBODY+NT,PFT/CT OR IMMUNOGLO
                BULIN+NT,PFT/CT
L77          993 SEA FILE=EMBASE ABB=ON  PLU=ON  L69 AND L76
L78           34 SEA FILE=EMBASE ABB=ON  PLU=ON  L77 AND L70
L79            4 SEA FILE=EMBASE ABB=ON  PLU=ON  L78 AND L72
```

```
=> d que L84
L67        2232 SEA FILE=EMBASE ABB=ON  PLU=ON  LYMPHOTOXIN+PFT/CT
L68        3301 SEA FILE=EMBASE ABB=ON  PLU=ON  TUMOR NECROSIS FACTOR RECEPTOR+
                PFT/CT
L69        5389 SEA FILE=EMBASE ABB=ON  PLU=ON  L67 OR L68
L70         301 SEA FILE=EMBASE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L72      281191 SEA FILE=EMBASE ABB=ON  PLU=ON  VIRUS+PFT/CT OR DNA VIRUS+NT,PF
                T/CT OR RNA VIRUS+NT,PFT/CT
L80         301 SEA FILE=EMBASE ABB=ON  PLU=ON  L69 (L) (AD OR DO OR DT OR PD
                OR PK)/CT
L81          17 SEA FILE=EMBASE ABB=ON  PLU=ON  L80 AND L70
L84           1 SEA FILE=EMBASE ABB=ON  PLU=ON  L81 AND L72

=> d que L85
L67        2232 SEA FILE=EMBASE ABB=ON  PLU=ON  LYMPHOTOXIN+PFT/CT
L68        3301 SEA FILE=EMBASE ABB=ON  PLU=ON  TUMOR NECROSIS FACTOR RECEPTOR+
                PFT/CT
L69        5389 SEA FILE=EMBASE ABB=ON  PLU=ON  L67 OR L68
L70         301 SEA FILE=EMBASE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L76      345967 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTIBODY+NT,PFT/CT OR IMMUNOGLO
                BULIN+NT,PFT/CT
L80         301 SEA FILE=EMBASE ABB=ON  PLU=ON  L69 (L) (AD OR DO OR DT OR PD
                OR PK)/CT
L81          17 SEA FILE=EMBASE ABB=ON  PLU=ON  L80 AND L70
L85           1 SEA FILE=EMBASE ABB=ON  PLU=ON  L81 AND L76

=> d que L91
L68        3301 SEA FILE=EMBASE ABB=ON  PLU=ON  TUMOR NECROSIS FACTOR RECEPTOR+
                PFT/CT
L70         301 SEA FILE=EMBASE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L86         115 SEA FILE=EMBASE ABB=ON  PLU=ON  TUMOR NECROSIS FACTOR BINDING
                PROTEIN/CT
L87           4 SEA FILE=EMBASE ABB=ON  PLU=ON  L86 AND L70
L88           3 SEA FILE=EMBASE ABB=ON  PLU=ON  L87 AND L68
L91           1 SEA FILE=EMBASE ABB=ON  PLU=ON  L88 AND HUMAN/CT

=> d que L93
L70         301 SEA FILE=EMBASE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L92           3 SEA FILE=EMBASE ABB=ON  PLU=ON  TUMOR NECROSIS FACTOR RECEPTOR
                BLOCKING AGENT/CT
L93           0 SEA FILE=EMBASE ABB=ON  PLU=ON  L70 AND L92

=> d que L95
L70         301 SEA FILE=EMBASE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L94           2 SEA FILE=EMBASE ABB=ON  PLU=ON  TUMOR NECROSIS FACTOR RECEPTOR
                DERIVATIVE/CT
L95           0 SEA FILE=EMBASE ABB=ON  PLU=ON  L70 AND L94

=> d que L99
L99           1 SEA FILE=EMBASE ABB=ON  PLU=ON  LYMPHOTOXIN BETA RECEPTOR
                IMMUNOGLOBULIN FUSION PROTEIN/CT
```

AD = Drug administration
DO - Drug Dosage
DT - Drug therapy
PD - Pharmacology
PK - Pharmacokinetics

```
=> d que L101
L1          362 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN (2A) BETA
L2          112 SEA FILE=MEDLINE ABB=ON  PLU=ON  L1 (3A) RECEPTOR
L45         117 SEA FILE=MEDLINE ABB=ON  PLU=ON  L2 OR (LYMPHOTOXIN BETA-SPECIF
                IC RECEPTOR OR LT.BETA.R OR LT-.BETA.R OR LT-.BETA-R)
L67        2232 SEA FILE=EMBASE ABB=ON  PLU=ON  LYMPHOTOXIN+PFT/CT
L68        3301 SEA FILE=EMBASE ABB=ON  PLU=ON  TUMOR NECROSIS FACTOR RECEPTOR+
                PFT/CT
L69        5389 SEA FILE=EMBASE ABB=ON  PLU=ON  L67 OR L68
L80         301 SEA FILE=EMBASE ABB=ON  PLU=ON  L69 (L) (AD OR DO OR DT OR PD
                OR PK)/CT
L100          9 SEA FILE=EMBASE ABB=ON  PLU=ON  L45 (3A) FUSION
L101          0 SEA FILE=EMBASE ABB=ON  PLU=ON  L80 AND L100


=> s l79 or l84 or l85 or l91 or l99
L175          8 L79 OR L84 OR L85 OR L91 OR L99

=> file hcaplus
FILE 'HCAPLUS' ENTERED AT 17:42:40 ON 24 JUN 2002
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FILE COVERS 1907 - 24 Jun 2002  VOL 136 ISS 26
FILE LAST UPDATED: 21 Jun 2002  (20020621/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> d que L119
L103        177 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOTOXIN (L) .BETA."+PFT/C
                T
L104         86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOKINE RECEPTORS (L)
                .BETA.-LYMPHOTOXIN"+PFT/CT
L105         48 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L103 (L) (THU OR BAC OR DMA
                OR PAC OR PKT)/RL
L106         17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L104 (L) (THU OR BAC OR DMA
                OR PAC OR PKT)/RL
L116          5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L105 AND L106
L117      75234 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SIGNAL TRANSDUCTION+NT,PFT/CT

L118          3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L116 AND L117
L119          1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L118 AND DRUGS/CT
```

THU - Therapeutic use
BAC - Biological activity
DMA - Drug mechanism of action
PAC - Pharmacological activity
PK - Pharmacokinetics

```
=> d que L129
L103        177 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOTOXIN (L) .BETA."+PFT/C
                T
L104         86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOKINE RECEPTORS (L)
                .BETA.-LYMPHOTOXIN"+PFT/CT
L124      70144 SEA FILE=HCAPLUS ABB=ON  PLU=ON  IMMUNOGLOBULINS/CT
L126        234 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L103 OR L104
L127         29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L126 AND VIRUS/OBI
L128       9351 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L124 (L) (THU OR BAC OR DMA
                OR PAC OR PKT)/RL
L129          3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L127 AND L128


=> d que L132
L103        177 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOTOXIN (L) .BETA."+PFT/C
                T
L104         86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOKINE RECEPTORS (L)
                .BETA.-LYMPHOTOXIN"+PFT/CT
L126        234 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L103 OR L104
L127         29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L126 AND VIRUS/OBI
L130     195688 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIBODIES+NT/CT
L131      31910 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L130 (L) (THU OR BAC OR DMA
                OR PAC OR PKT)/RL
L132          3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L127 AND L131


=> d que L134
L103        177 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOTOXIN (L) .BETA."+PFT/C
                T
L104         86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOKINE RECEPTORS (L)
                .BETA.-LYMPHOTOXIN"+PFT/CT
L126        234 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L103 OR L104
L127         29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L126 AND VIRUS/OBI
L133      10659 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "FUSION PROTEINS (CHIMERIC
                PROTEINS)"+PFT/CT
L134          3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L127 AND L133


=> d que L139
L103        177 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOTOXIN (L) .BETA."+PFT/C
                T
L104         86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOKINE RECEPTORS (L)
                .BETA.-LYMPHOTOXIN"+PFT/CT
L124      70144 SEA FILE=HCAPLUS ABB=ON  PLU=ON  IMMUNOGLOBULINS/CT
L126        234 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L103 OR L104
L128       9351 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L124 (L) (THU OR BAC OR DMA
                OR PAC OR PKT)/RL
L130     195688 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIBODIES+NT/CT
L131      31910 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L130 (L) (THU OR BAC OR DMA
                OR PAC OR PKT)/RL
L133      10659 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "FUSION PROTEINS (CHIMERIC
                PROTEINS)"+PFT/CT
L136       3838 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L133 (L) (THU OR BAC OR DMA
                OR PAC OR PKT)/RL
L137         10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L126 AND L136
L138          8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L137 AND L131
L139          7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L128 AND L138
```

```
=> d que L143
L103        177 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOTOXIN (L) .BETA."+PFT/C
                T
L104         86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOKINE RECEPTORS (L)
                .BETA.-LYMPHOTOXIN"+PFT/CT
L126        234 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L103 OR L104
L141      33586 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIVIRAL AGENTS+NT,PFT/CT
L142          3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L126 AND L141
L143          2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L142 NOT APOPTOSIS-INDUCING
                MOLECULE II/TI


=> d que L148
L103        177 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOTOXIN (L) .BETA."+PFT/C
                T
L104         86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOKINE RECEPTORS (L)
                .BETA.-LYMPHOTOXIN"+PFT/CT
L126        234 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L103 OR L104
L144      76575 SEA FILE=HCAPLUS ABB=ON  PLU=ON  INFECTION+NT,PFT/CT
L146         60 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L126 (L) (THU OR BAC OR DMA
                OR PAC OR PKT)/RL
L147          5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L146 AND L144
L148          1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L147 AND IMMUNITY+NT,PFT/CT


=> d que L150
L103        177 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOTOXIN (L) .BETA."+PFT/C
                T
L104         86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LYMPHOKINE RECEPTORS (L)
                .BETA.-LYMPHOTOXIN"+PFT/CT
L126        234 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L103 OR L104
L146         60 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L126 (L) (THU OR BAC OR DMA
                OR PAC OR PKT)/RL
L149      10125 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "SHOCK (CIRCULATORY COLLAPSE)"
                +NT,PFT/CT
L150          2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L146 AND L149


=> S l119 or l129 or l132 or l134 or l139 or l143 or l148 or l150
L176         11 L119 OR L129 OR L132 OR L134 OR L139 OR L143 OR L148 OR L150

=> FIL WPIDS
FILE 'WPIDS' ENTERED AT 17:46:55 ON 24 JUN 2002
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FILE LAST UPDATED: 21 JUN 2002              <20020621/UP>
MOST RECENT DERWENT UPDATE            200239   <200239/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> The BATCH option for structure searches has been
    enabled in WPINDEX/WPIDS and WPIX  >>>

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    TRADE USER GUIDE, PLEASE VISIT:
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http://www.derwent.com/data/stn3.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT: http://www.derwent.com/userguides/dwpi_guide.html <<<

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=> d que L159
L151          80 SEA FILE=WPIDS ABB=ON  PLU=ON  LYMPHOTOXIN (3A) BETA OR LTB OR
                 LT.BETA. OR LT-.BETA.
L152       38278 SEA FILE=WPIDS ABB=ON  PLU=ON  VIRUS OR VIRAL?
L153          16 SEA FILE=WPIDS ABB=ON  PLU=ON  L151 AND L152
L154      991230 SEA FILE=WPIDS ABB=ON  PLU=ON  ANTAG? OR INHIBIT? OR BLOCK? OR
                 REVERS?
L155          10 SEA FILE=WPIDS ABB=ON  PLU=ON  L153 AND L154
L159           5 SEA FILE=WPIDS ABB=ON  PLU=ON  L155 AND (VIRUS OR VIRAL? OR
                 INFECT?)/TI


=> d que L163
L161         166 SEA FILE=WPIDS ABB=ON  PLU=ON  LYMPHOTOXIN BETA-SPECIFIC
                 RECEPTOR OR TNF-.BETA. RECEPTOR OR TUMOR NECROSIS FACTOR
                 RECEPTOR OR LT-.BETA.R OR LT-.BETA.-R OR LT.BETA.R OR TNF-.BETA
                 .R OR TNF-R OR TNFR
L162          14 SEA FILE=WPIDS ABB=ON  PLU=ON  L161 (3A) SOLUBL?
L163           1 SEA FILE=WPIDS ABB=ON  PLU=ON  L162 AND (VIRUS OR VIRAL?)


=> d que L165
L151          80 SEA FILE=WPIDS ABB=ON  PLU=ON  LYMPHOTOXIN (3A) BETA OR LTB OR
                 LT.BETA. OR LT-.BETA.
L161         166 SEA FILE=WPIDS ABB=ON  PLU=ON  LYMPHOTOXIN BETA-SPECIFIC
                 RECEPTOR OR TNF-.BETA. RECEPTOR OR TUMOR NECROSIS FACTOR
                 RECEPTOR OR LT-.BETA.R OR LT-.BETA.-R OR LT.BETA.R OR TNF-.BETA
                 .R OR TNF-R OR TNFR
L164           4 SEA FILE=WPIDS ABB=ON  PLU=ON  L161 (3A) (FUSION OR CHIMERIC)
L165           1 SEA FILE=WPIDS ABB=ON  PLU=ON  L151 AND L164


=> d que L169
L161         166 SEA FILE=WPIDS ABB=ON  PLU=ON  LYMPHOTOXIN BETA-SPECIFIC
                 RECEPTOR OR TNF-.BETA. RECEPTOR OR TUMOR NECROSIS FACTOR
                 RECEPTOR OR LT-.BETA.R OR LT-.BETA.-R OR LT.BETA.R OR TNF-.BETA
                 .R OR TNF-R OR TNFR
L168           2 SEA FILE=WPIDS ABB=ON  PLU=ON  L161 (3A) (IG? OR IMMUNOGLOB?)
                 (5A) (FUSION OR CHIMERIC)
L169           1 SEA FILE=WPIDS ABB=ON  PLU=ON  L168 NOT EXTRACELLULAR RECOVERY/
                 TI


=> d que L173
L151          80 SEA FILE=WPIDS ABB=ON  PLU=ON  LYMPHOTOXIN (3A) BETA OR LTB OR
                 LT.BETA. OR LT-.BETA.
L152       38278 SEA FILE=WPIDS ABB=ON  PLU=ON  VIRUS OR VIRAL?
L153          16 SEA FILE=WPIDS ABB=ON  PLU=ON  L151 AND L152
L171       48665 SEA FILE=WPIDS ABB=ON  PLU=ON  ANTIBOD? OR ANTI BOD? OR
                 IMMUNOGLOB?
L172           9 SEA FILE=WPIDS ABB=ON  PLU=ON  L153 AND L171
L173           5 SEA FILE=WPIDS ABB=ON  PLU=ON  L172 AND (VIRUS OR INFECTION)/TI
```

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=> s l159 or l163 or l169 or l173
L177          7 L159 OR L163 OR L169 OR L173


=> dup rem L174 L175 L176 L177
FILE 'MEDLINE' ENTERED AT 17:48:54 ON 24 JUN 2002

FILE 'EMBASE' ENTERED AT 17:48:54 ON 24 JUN 2002
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FILE 'HCAPLUS' ENTERED AT 17:48:54 ON 24 JUN 2002
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PROCESSING COMPLETED FOR L174
PROCESSING COMPLETED FOR L175
PROCESSING COMPLETED FOR L176
PROCESSING COMPLETED FOR L177
L178          30 DUP REM L174 L175 L176 L177 (6 DUPLICATES REMOVED)

=> d ibib ab ct 1-30

L178 ANSWER 1 OF 30  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:293705  HCAPLUS
DOCUMENT NUMBER:          136:324074
TITLE:                    Humanized anti-lymphotoxin .beta. receptor
                          (LT-.beta.-R) antibodies for treating tumor
INVENTOR(S):              Garber, Ellen; Lyne, Paul; Saldanha, Jose W.
PATENT ASSIGNEE(S):       Biogen, Inc., USA
SOURCE:                   PCT Int. Appl., 41 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     WO 2002030986      A2   20020418      WO 2001-US32140  20011012
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
             US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                  US 2000-240285P  P  20001013
                                        US 2001-275289P  P  20010313
                                        US 2001-299987P  P  20010621
AB   LT-.alpha.-R-specific humanized murine CBE11 antibodies and fragments are
     provided.  The humanized antibodies of this invention are linked to an
     immunotoxin (e.g. ricin A chain of Pseudomonas toxin), chemotherapeutic
     agent (e.g. adriamycin, 5-FU, vinblastine, actinomycin D, etoposide,
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cisplatin, methotrexate and doxorubicin), a radioisotope, or a cytotoxic factor (e.g. TNF-.alpha., TNF-.beta., IL-1, INF-.gamma., and IL-2) for treating cancer in human patients.
CT Ricins
CT **Immunoglobulins**
CT **Immunoglobulins**
CT **Immunoglobulins**
CT Hybridoma
CT Hybridoma
CT **Immunoglobulins**
CT **Immunoglobulins**
CT **Immunoglobulins**
CT **Immunoglobulins**
CT **Immunoglobulins**
CT **Immunoglobulins**
CT Toxins
CT Drug delivery systems
CT Radionuclides, biological studies
CT **Immunoglobulins**
CT **Immunoglobulins**
CT Antitumor agents
CT Chemotherapy
CT DNA sequences
CT Human
CT Mammal (Mammalia)
CT Molecular cloning
CT Protein sequences
CT **Antibodies**
CT Cytokines
CT Interleukin 1
CT Interleukin 2
CT **Lymphotoxin**
CT Nucleic acids
CT Tumor necrosis factors
CT **Fusion proteins (chimeric proteins)**
CT Drug delivery systems
CT Drug delivery systems
CT **Immunoglobulins**
CT **Antibodies**
CT Pseudomonas
CT **Lymphokine receptors**
CT Interferons

L178 ANSWER 2 OF 30 MEDLINE
ACCESSION NUMBER: 2002052009 MEDLINE
DOCUMENT NUMBER: 21636514 PubMed ID: 11777992
TITLE: Nonmitogenic CD3 antibody reverses **virally** induced (rat insulin promoter-lymphocytic choriomeningitis **virus**) autoimmune diabetes without impeding **viral** clearance.
AUTHOR: von Herrath Matthias G; Coon Bryan; Wolfe Tom; Chatenoud Lucienne
CORPORATE SOURCE: Department of Immune Regulation, La Jolla Institute for Allergy and Immunology, San Diego, CA 92121, USA.. matthias@liai.org
CONTRACT NUMBER: AI44451 (NIAID)
DK510791 (NIDDK)
U19 AI51973 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGY, (2002 Jan 15) 168 (2) 933-41.
Journal code: 2985117R. ISSN: 0022-1767.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020201
Entered Medline: 20020131

AB Treatment with nonmitogenic CD3 Ab reverses established autoimmune diabetes in nonobese diabetic mice by restoring self-tolerance, and is currently under clinical evaluation in patients presenting recent onset type I diabetes. Due to the immunosuppressive potential of this strategy, it was relevant to explore how this treatment would influence the outcome of concomitant **viral** infections. In this study, we used a transgenic model of **virally** induced autoimmune diabetes (rat insulin promoter-lymphocytic choriomeningitis **virus**) that allows for more precise tracking of the autoaggressive response and choice of the time point for initiation of autoimmunity. CD3 was most effective during a clearly defined prediabetic phase and prevented up to 100% of diabetes by drastically lowering activation of autoaggressive CD8 lymphocytes and their production of inflammatory cytokines. Interestingly, reversion of established disease could be achieved as well, when nonmitogenic CD3 was administered late during pathogenesis to overtly diabetic recipients. Most importantly, competence to clear **viral** infections was maintained. Thus, administration of nonmitogenic CD3 prevents diabetes by sufficient systemic reduction of (auto)aggressive lymphocytes, but without compromising antiviral immune competence.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Adjuvants, Immunologic: PD, pharmacology
Adoptive Transfer
Antibodies, Monoclonal: ME, metabolism
***Antibodies, Monoclonal: TU, therapeutic use**
*Antigens, CD3: IM, immunology
Arenaviridae Infections: IM, immunology
Arenaviridae Infections: PC, prevention & control
Arenaviridae Infections: VI, virology
Binding Sites, Antibody
CD4-Positive T-Lymphocytes: IM, immunology
CD4-Positive T-Lymphocytes: ME, metabolism
Cell Division: IM, immunology
Cell Movement: IM, immunology
Diabetes Mellitus, Insulin-Dependent: IM, immunology
Diabetes Mellitus, Insulin-Dependent: PA, pathology
*Diabetes Mellitus, Insulin-Dependent: PC, prevention & control
*Diabetes Mellitus, Insulin-Dependent: VI, virology
Immunoglobulins, Fab: ME, metabolism
Immunoglobulins, Fab: PD, pharmacology
*Insulin: GE, genetics
Insulin: IM, immunology
Interleukin-4: BI, biosynthesis
Islets of Langerhans: IM, immunology
Islets of Langerhans: PA, pathology
Lymphocyte Count
Lymphocyte Transformation: IM, immunology
Lymphocytes: CY, cytology
Lymphocytes: IM, immunology
***Lymphocytic choriomeningitis virus: GE, genetics**
Lymphocytic choriomeningitis virus: IM, immunology
Lymphotoxin: AI, antagonists & inhibitors
Membrane Proteins: AI, antagonists & inhibitors

Mice
Mice, Inbred C57BL
Mice, Transgenic
Mitogens: PD, pharmacology
*Promoter Regions (Genetics): IM, immunology
Rats
Receptors, Fc: ME, metabolism
Spleen: CY, cytology
Spleen: IM, immunology
Spleen: ME, metabolism
Spleen: TR, transplantation
Tumor Necrosis Factor: AI, antagonists & inhibitors
Viral Proteins: GE, genetics

L178 ANSWER 3 OF 30 MEDLINE
ACCESSION NUMBER: 2002134149 MEDLINE
DOCUMENT NUMBER: 21843386 PubMed ID: 11854328
TITLE: Blockade of LIGHT/LTbeta and CD40 signaling induces allospecific T cell anergy, preventing graft-versus-host disease.
AUTHOR: Tamada Koji; Tamura Hideto; Flies Dallas; Fu Yang-Xin; Celis Esteban; Pease Larry R; Blazar Bruce R; Chen Lieping
CORPORATE SOURCE: Department of Immunology, Mayo Clinic, Rochester, Minnesota 55905, USA.
CONTRACT NUMBER: AI-34495 (NIAID)
AI-35225 (NIAID)
CA-79915 (NCI)
CA85721 (NCI)
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (2002 Feb) 109 (4) 549-57.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020301
Last Updated on STN: 20020322
Entered Medline: 20020321

AB Previous studies have shown that blockade of LIGHT, a T cell costimulatory molecule belonging to the TNF superfamily, by **soluble lymphotoxin beta receptor**-Ig (LTbetaR-Ig) inhibits the cytotoxic T lymphocyte (CTL) response to host antigenic disparities and ameliorates lethal graft-versus-host disease (GVHD) in a B6 to BDF1 mouse model. Here, we demonstrate that infusion of an mAb against CD40 ligand (CD40L) further increases the efficacy of LTbetaR-Ig, leading to complete prevention of GVHD. We further demonstrate that alloantigen-specific CTLs become anergic upon rapid expansion, and persist in the tolerized mice as a result of costimulatory blockade. Transfer of anergic CTLs to secondary F1 mice fails to induce GVHD despite the fact that anergic CTLs can be stimulated to proliferate in vitro by antigens and cytokines. Our study provides a potential new approach for the prevention of lethal GVHD.

CT Check Tags: Animal; Female; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Antibodies, Monoclonal: PD, pharmacology
*CD40 Ligand: IM, immunology
Clonal Anergy
Graft vs Host Disease: ET, etiology
Graft vs Host Disease: IM, immunology

*Graft vs Host Disease: PC, prevention & control
Immunosuppression: MT, methods
Isoantigens
***Lymphotoxin: AI, antagonists & inhibitors**
*Membrane Proteins: AI, antagonists & inhibitors
Mice
Mice, Congenic
Mice, Inbred C57BL
Mice, Inbred DBA
Mice, Transgenic
*T-Lymphocytes: IM, immunology
T-Lymphocytes, Cytotoxic: IM, immunology
*Tumor Necrosis Factor: AI, antagonists & inhibitors

L178 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2001:781125 HCAPLUS
DOCUMENT NUMBER: 135:343309
TITLE: Ligand p30/LIGHT for HVEM (herpes **virus** entry mediator) and methods of therapeutic use
INVENTOR(S): Ware, Carl F.
PATENT ASSIGNEE(S): La Jolla Institute for Allergy and Immunology, USA
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079496	A2	20011025	WO 2001-US11857	20010411

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-524325 A2 20000313
US 2000-549096 A 20000412

AB A novel polypeptide ligand, p30, for HVEM (herpes virus entry mediator) and functional variations and fragments thereof are provided. The HVEM ligand is isolated from II-23.D7 cell line, a human CD4+ T cell hybridoma. P30, which can be found as a membrane protein and can function as a cytokine, is also called LIGHT, because this polypeptide is homologous to Lymphotoxins, exhibits Inducible expression, and competes with HSV Glycoprotein D for HVEM, a receptor expressed by T lymphocytes. Because LIGHT can compete with HSV glycoprotein D for HVEM, homo-trimeric sol. forms of this polypeptide can be used to block the entry of herpesvirus into cells. P30 is useful for modulating immune responses and in inhibiting infection and/or subsequent proliferation by herpesvirus. LIGHT also bind to the lymphotoxin-.beta. receptor (LT.beta.R). The present invention is also based upon the discovery that HVEM polypeptides have an antagonistic effect on inflammation. In particular, HVEM fusion proteins are capable of inhibiting inflammation when administered to a subject. HVEM-Fc fusion proteins are also provided. Methods for treating subjects with lymphoid cell disorders, tumors, autoimmune diseases, inflammatory disorders of those having or suspected of having a herpes

virus infection, utilizing p30 and the fusion proteins of the invention, are also provided.

CT Lymphoma
CT Receptors
CT Lymphotoxin
CT Gammaherpesvirinae
CT Herpesviridae
CT Human herpesvirus
CT Human herpesvirus 4
CT Human herpesvirus 5
CT Genetic vectors
CT Cytokines
CT Lymphoma
CT Lymphocyte
CT **Antibodies**
CT **Antibodies**
CT Neoplasm
CT Immunity
CT cDNA sequences
CT **Immunoglobulins**
CT Glycoproteins, specific or class
CT Cell activation
CT Inflammation
CT Drug delivery systems
CT Diabetes mellitus
CT Antitumor agents
CT **Antiviral agents**
CT Immunomodulators
CT Molecular cloning
CT Drug delivery systems
CT Signal transduction, biological
CT Transplant and Transplantation
CT Lymphokine receptors
CT Animal cell
CT Autoimmune disease
CT Leukemia
CT Multiple sclerosis
CT Myasthenia gravis
CT Rheumatoid arthritis
CT Protein sequences
CT **Fusion proteins (chimeric proteins)**
CT Drugs
CT Lymphocyte
CT Lupus erythematosus
CT Protein motifs
CT Growth, microbial
CT Infection
CT **Lymphokine receptors**

L178 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:435124 HCAPLUS
DOCUMENT NUMBER: 135:45182
TITLE: Multimeric forms of TNF superfamily ligands
INVENTOR(S): Kornbluth, Richard S.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042298	A1	20010614	WO 2000-US7380	20000320

W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1999-454223 A 19991209

AB A method for constructing stable bioactive fusion proteins of the difficult to express tumor necrosis factor superfamily (TNFSF), and particularly members CD40L (CD154) and RANKL/TRANCE, with collectins, particularly pulmonary surfactant protein D (SPD) is described. Single trimers of these proteins lack the full stimulatory efficacy of the natural membrane forms of these proteins in many cases. The multimeric nature of these sol. fusion proteins enables them to engage multiple receptors on the responding cells, thereby, mimicking the effects of the membrane forms of these ligands. For CD40L-SPD, the resulting protein stimulates B cells, macrophages, and dendritic cells, indicating its potential usefulness as a vaccine adjuvant. The large size of these fusion proteins makes them less likely to diffuse into the circulation, thereby limiting their potential systemic toxicity. This property may be esp. useful when these proteins are injected locally as a vaccine adjuvant or tumor immunotherapy agent to prevent them from diffusing away. In addn., these and other TNFSF-collecting fusion proteins present new possibilities for the expression of highly active, multimeric, sol. TNFSF members.

CT Glycoproteins, specific or class
CT Antigens
CT Cytokines
CT Surfactant proteins (pulmonary)
CT Tumor necrosis factors
CT Tumor necrosis factors
CT Tumor necrosis factors
CT Immunostimulants
CT Neoplasm
CT Agglutinins and Lectins
CT Lymphocyte
CT Human immunodeficiency **virus**
CT Proteins, general, biological studies
CT Alfalfa (Medicago sativa)
CT Animal
CT Antitumor agents
CT B cell (lymphocyte)
CT DNA sequences
CT Dendritic cell
CT Escherichia coli
CT Eukaryote (Eukaryotae)
CT Genetic vectors
CT Immunotherapy
CT Macrophage
CT Mammal (Mammalia)
CT Molecular cloning
CT Plant (Embryophyta)
CT Prokaryote
CT Protein sequences
CT Saccharomyces cerevisiae
CT Tobacco
CT Vaccines
CT Yeast

CT **Fusion proteins (chimeric proteins)**
CT Lymphotoxin
CT Animal cell
CT Receptors
CT Gene
CT DNA
CT Genetic element
CT Gene, animal
CT Tumor necrosis factors
CT Promoter (genetic element)
CT Vaccines
CT Antitumor agents
CT **Lymphotoxin**
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L178 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:265459 HCAPLUS
DOCUMENT NUMBER: 134:290751
TITLE: Recombinant single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders
INVENTOR(S): Halkier, Torben; Schambye, Hans Thalsgard; Okkels, Jens Sigurd; Andersen, Kim Vilbour; Nissen, Torben Lauesgaard; Soni, Bobby; Jeppesen, Claus Bekker; Van Den Hazel, Bart
PATENT ASSIGNEE(S): Maxygen Aps, Den.
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001025277	A1	20010412	WO 2000-DK563	20001006

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
DK 1999-1438 A 19991007
DK 1999-1855 A 19991223
DK 2000-1119 A 20000720

AB The invention relates to a single-chain oligomeric protein antagonist which binds to an extracellular ligand-binding domain of a cellular receptor of a type requiring binding of an oligomeric ligand to two or more receptor subunits to be activated, the protein comprising at least two, typically structurally homologous, receptor-binding sites of which at least one is capable of binding to a ligand-binding domain of the cellular receptor and at least one is incapable of effectively binding to a ligand-binding domain of the cellular receptor, whereby the single-chain oligomeric protein is capable of binding to the receptor, but incapable of activating the receptor; as well as to nucleotide sequences encoding such single-chain oligomeric proteins, expression vectors comprising such a nucleotide sequence, recombinant host cells comprising such a nucleotide

sequence or expression vector, methods for producing the nucleotide sequences and proteins, pharmaceutical compns. comprising the single-chain oligomeric protein, and use of the single-chain oligomeric protein for the prodn. of medicaments and in therapy. A preferred single-chain antagonist according to the invention is a TNF-.alpha. antagonist. Thus, a single-chain TNF-.alpha. protein comprising of 3 human TNF-.alpha. chains connected by linker peptides was produced with Saccharomyces cerevisiae and shown to be an agonist of the TNF-.alpha. receptor. The same TNF-.alpha. trimer contg. Y87R mutations in the first and third copies of TNF-.alpha. was also prepd. This was shown to be a partial TNF-.alpha. agonist and a competitive antagonist of the TNF-.alpha. receptor.

CT Bone morphogenetic proteins
CT Bone morphogenetic proteins
CT Bone morphogenetic proteins
CT Proteins, specific or class
CT Bone morphogenetic proteins
CT Bone morphogenetic proteins
CT Bone morphogenetic proteins
CT Bone morphogenetic proteins
CT Cytokines
CT CD antigens
CT Glycoproteins, specific or class
CT Intestine, disease
CT Antigens
CT Growth factors, animal
CT Proteins, specific or class
CT Granulomatous disease
CT Spinal column
CT Antiarteriosclerotics
CT Receptors
CT Heart, disease
CT Brain, disease
CT CD30 (antigen)
CT Molecular cloning
CT Tumor necrosis factor receptors
CT Tumor necrosis factor receptors
CT Arthritis
CT Anti-inflammatory agents
CT Antirheumatic agents
CT Cachexia
CT Diabetes mellitus
CT Myasthenia gravis
CT Psoriasis
CT Sjogren's syndrome
CT Cytokine receptors
CT Growth factor receptors
CT Tumor necrosis factor receptors
CT **Shock (circulatory collapse)**
CT **Lymphotoxin**
CT Fas ligand
CT Interleukin 10
CT Interleukin 16
CT Platelet-derived growth factors
CT Tumor necrosis factors
CT Surgery
CT Lupus erythematosus
CT Eye, disease
CT Receptors
CT Transforming growth factors
CT Transforming growth factors

CT Transforming growth factors
CT Transforming growth factors
CT Interferons
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L178 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:630070 HCAPLUS
DOCUMENT NUMBER: 135:317407
TITLE: Elimination of colonic patches with lymphotoxin .beta. receptor-Ig prevents Th2 cell-type colitis
AUTHOR(S): Dohi, Taeko; Rennert, Paul D.; Fujihashi, Kohtaro; Kiyono, Hiroshi; Shirai, Yuko; Kawamura, Yuki I.; Browning, Jeffrey L.; McGhee, Jerry R.
CORPORATE SOURCE: Department of Gastroenterology, Research Institute, International Medical Center of Japan, Tokyo, 162-8655, Japan
SOURCE: Journal of Immunology (2001), 167(5), 2781-2790
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Past studies have shown that colonic patches, which are the gut-assocd. lymphoreticular tissues (GALT) in the colon, become much more pronounced in hapten-induced murine colitis, and this was assocd. with Th2-type T cell responses. To address the role of GALT in colonic inflammation, exptl. colitis was induced in mice either lacking organized GALT or with altered GALT structures. Trinitrobenzene sulfonic acid was used to induce colitis in mice given lymphotoxin-.beta. receptor-Ig fusion protein (LT.beta.R-Ig) in utero, a treatment that blocked the formation of both Peyer's and colonic patches. Mice deficient in colonic patches developed focal acute ulcers with Th1-type responses, whereas lesions in normal mice were of a diffuse mucosal type with both Th1- and Th2-type cytokine prodn. We next detd. whether LT.beta.R-Ig could be used to treat colitis in normal or Th2-dominant, IFN-.gamma. gene knockout (IFN-.gamma.-/-) mice. Four weekly treatments with LT.beta.R-Ig resulted in deletion of Peyer's and colonic patches with significant decreases in nos. of dendritic cells. This pretreatment protected IFN-.gamma.-/- mice from trinitrobenzene sulfonic acid-induced colitis; however, in normal mice this weekly treatment was less protective. In these mice hypertrophy of colonic patches was seen after induction of colitis. We conclude that Th2-type colitis is dependent upon the presence of colonic patches. The effect of LT.beta.R-Ig was mediated through prevention of colonic patch hypertrophy in the absence of IFN-.gamma.. Thus, LT.beta.R-Ig may offer a possible treatment for the Th2-dominant form of colitis.
CT **Fusion proteins (chimeric proteins)**
CT Intestine, disease
CT Inflammation
CT Cytokines
CT **Immunoglobulins**
CT Lymphatic system
CT T cell (lymphocyte)
CT **Lymphokine receptors**
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L178 ANSWER 8 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001122609 EMBASE
TITLE: Effect of mature lymphocytes and lymphotoxin on the development of the follicle-associated epithelium and M

cells in mouse peyer's patches.

AUTHOR: Debard N.; Sierro F.; Browning J.; Kraehenbuhl J.-P.
CORPORATE SOURCE: Dr. N. Debard, ISREC, CH-1066 Epalinges, Switzerland. Nathalie.Debard@isrec.unil.ch

SOURCE: Gastroenterology, (2001) 120/5 (1173-1182).
Refs: 45
ISSN: 0016-5085 CODEN: GASTAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
029 Clinical Biochemistry
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background & Aims: Mechanisms regulating M-cell formation are still poorly understood. In vitro studies showed that lymphocytes trigger the conversion of enterocyte cell lines into M cell-like cells on coculture, whereas in vivo their role in M cell differentiation is still elusive. Our aim was first to examine Rag-1-/- mice, lacking B and T lymphocytes, for the presence of intestinal M Cells. Second, we investigated the role of lymphotoxin .alpha..beta. signaling on M-cell formation, given its pivotal role in the development of mouse Peyer's patches. Methods: Small intestines of Rag-1-/- mice, injected or not with soluble lymphotoxin .beta. receptor-immunoglobulin fusion Protein, were analyzed morphologically using whole mount cytochemical staining, immunohistochemistry, and electron microscopy. Results: Small Peyer's patch-like aggregates were found in Rag1-/- mice in normal number and location. The overlying epithelium of such aggregates was reduced in size but still harbored M cells. In vivo neutralization of lymphotoxin .beta.-receptor signaling partially reduced the percentage of M cells. . Conclusions: The absence of mature lymphocytes does not prevent the formation of M cells indicating that the signaling molecules that support M-cell differentiation, such as lymphotoxin .alpha..beta., may also be supplied by non-B and non-T cells. Mature B lymphocytes, however, are required for the formation of a full-sized follicle-associated epithelium.

CT Medical Descriptors:
*cell maturation
lymphocyte
coculture
intestine cell
B lymphocyte
T lymphocyte
cell differentiation
small intestine
Peyer patch
cytochemistry
immunohistochemistry
electron microscopy
cell aggregation
cell size
intestine epithelium
cell count
cellular distribution
nonhuman
mouse
controlled study
animal tissue
animal cell
article

priority journal
Drug Descriptors:
*lymphotoxin: IP, intraperitoneal drug administration
***lymphotoxin beta receptor immunoglobulin fusion protein: IP, intraperitoneal drug administration**
unclassified drug

L178 ANSWER 9 OF 30 MEDLINE
ACCESSION NUMBER: 2001567231 MEDLINE
DOCUMENT NUMBER: 21527032 PubMed ID: 11672543
TITLE: Lymphotoxins and cytomegalovirus cooperatively induce interferon-beta, establishing host-virus detente.
AUTHOR: Benedict C A; Banks T A; Senderowicz L; Ko M; Britt W J; Angulo A; Ghazal P; Ware C F
CORPORATE SOURCE: Division of Molecular Immunology, La Jolla Institute for Allergy and Immunology, San Diego, CA 92121, USA.
CONTRACT NUMBER: AI30627 (NIAID)
AI33068 (NIAID)
AI35602 (NIAID)
AI44851 (NIAID)
SOURCE: IMMUNITY, (2001 Oct) 15 (4) 617-26.
Journal code: 9432918. ISSN: 1074-7613.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011024
Last Updated on STN: 20020122
Entered Medline: 20011204

AB Tumor necrosis factor (TNF)-related cytokines regulate cell death and survival and provide strong selective pressures for viruses, such as cytomegalovirus (CMV), to evolve counterstrategies in order to persist in immune-competent hosts. Signaling by the **lymphotoxin** (LT)-**beta** receptor or TNF receptor-1, but not Fas or TRAIL receptors, inhibits the cytopathicity and replication of human CMV by a nonapoptotic, reversible process that requires nuclear factor kappa B (NF-kappa B)-dependent induction of interferon-beta (IFN-beta). Efficient induction of IFN-beta requires virus infection and LT signaling, demonstrating the need for both host and viral factors in the curtailment of viral replication without cellular elimination. LT alpha-deficient mice and LT beta R-Fc transgenic mice were profoundly susceptible to murine CMV infection. Together, these results reveal an essential and conserved role for LTs in establishing host defense to CMV.

CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
Carrier Proteins: PH, physiology
Cells, Cultured
Cytomegalovirus: GD, growth & development
Cytomegalovirus: PY, pathogenicity
***Cytomegalovirus: PH, physiology**
Herpesviridae Infections: ET, etiology
*Host-Parasite Relations
***Interferon-beta: BI, biosynthesis**
Interferon-beta: GE, genetics
Interferon-beta: PH, physiology
Lymphotoxin: GE, genetics
***Lymphotoxin: PD, pharmacology**
*Membrane Proteins: PD, pharmacology
Mice
Mice, Transgenic

Muromegalovirus
NF-kappa B: PH, physiology
Proteins: PH, physiology
RNA, Messenger: BI, biosynthesis
Receptors, Tumor Necrosis Factor: GE, genetics
Survival Rate
*Trans-Activation (Genetics)
*Tumor Necrosis Factor: PD, pharmacology
Virus Replication: DE, drug effects

L178 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 2000:260054 HCAPLUS
DOCUMENT NUMBER: 132:292716
TITLE: Reversal of viral-induced systemic shock and respiratory distress by blockade of the lymphotoxin .beta. pathway
INVENTOR(S): Browning, Jeff; Puglielli, Maryann; Ahmed, Rafi
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021558	A1	20000420	WO 1999-US23477	19991008
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9962964	A1	20000501	AU 1999-62964	19991008
EP 1119370	A1	20010801	EP 1999-950270	19991008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9915025	A	20010814	BR 1999-15025	19991008
NO 2001001757	A	20010608	NO 2001-1757	20010406
US 2002001585	A1	20020103	US 2001-829031	20010409
PRIORITY APPLN. INFO.:			US 1998-103662P P	19981009
			WO 1999-US23477 W	19991008

AB This invention provides methods of inducing an antiviral response in an individual comprising administering to the individual an effective amt. of a LT-.beta. blocking agent and a pharmaceutically acceptable carrier. In particular this invention provides methods for treating viral-induced systemic shock and respiratory distress. The LT-.beta. inhibitor is an anti-LT-.beta. antibody, sol. LT-.beta. receptor, or fusion protein contg. LT-.beta. receptor and Ig.
CT Lymphocytic choriomeningitis **virus**
CT Proteins, specific or class
CT **Signal transduction, biological**
CT **Immunoglobulins**
CT **Immunoglobulins**
CT Human herpesvirus
CT **Fusion proteins (chimeric proteins)**

CT **Drugs**
CT Dengue **virus**
CT Ebola **virus**
CT Lassa **virus**
CT Marburg **virus**
CT Sin Nombre hantavirus
CT **Antibodies**
CT **Shock (circulatory collapse)**
CT Infection
CT **Lymphotoxin**
CT **Lymphokine receptors**
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L178 ANSWER 11 OF 30 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-672707 [65] WPIDS
CROSS REFERENCE: 2001-550072 [58]
DOC. NO. CPI: C2000-203785
TITLE: Use of a **soluble tumor necrosis factor receptor**, specifically TNFR Fc for the treatment of medical disorders, especially ordinary psoriasis.
DERWENT CLASS: B04
INVENTOR(S): PLUENNEKE, J D; FINCK, B K
PATENT ASSIGNEE(S): (IMMV) IMMUNEX CORP; (PLUE-I) PLUENNEKE J D
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000062790	A2	20001026	(200065)*	EN	30
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000043632	A	20001102	(200107)		
US 2001021380	A1	20010913	(200155)		
AU 2001045336	A	20010903	(200202)		
EP 1171148	A2	20020116	(200207)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000062790	A2		WO 2000-US10565	20000419
AU 2000043632	A		AU 2000-43632	20000419
US 2001021380	A1	Provisional	US 1999-130074P	19990419
		Provisional	US 1999-134320P	19990514
		Provisional	US 1999-143959P	19990715
		Provisional	US 1999-148234P	19990811
		CIP of	US 1999-373828	19990813
		Provisional	US 1999-164676P	19991110
		Provisional	US 2000-184864P	20000225
		CIP of	WO 2000-US10565	20000419
		CIP of	US 2000-602351	20000623
		CIP of	US 2000-726781	20001129

	US 2001-778403	20010207
AU 2001045336 A	AU 2001-45336	20010222
EP 1171148 A2	EP 2000-923525	20000419
	WO 2000-US10565	20000419

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000043632 A		Based on	WO 200062790
AU 2001045336 A		Based on	WO 200162272
EP 1171148	A2	Based on	WO 200062790

PRIORITY APPLN. INFO: US 2000-184864P 20000225; US 1999-130074P 19990419; US 1999-134320P 19990514; US 1999-143959P 19990715; US 1999-148234P 19990811; US 1999-373828 19990813; US 1999-164676P 19991110; US 2000-602351 20000623; US 2000-726781 20001129; US 2001-778403 20010207

AB WO 200062790 A UPAB: 20020130
NOVELTY - Treatment of ordinary psoriasis comprises administration of a soluble tumor necrosis factor (TNF) receptor.

ACTIVITY - Dermatological; antibacterial; antiviral; protozoacide; analgesic; cardiant; hemotropic; cytostatic; nootropic; anticonvulsant; hepatotropic; antirheumatic; osteopathic; immunosuppressive; anorectic; gynecological.

Sixty patients with active psoriatic arthritis were enrolled in a double-blind, randomized, placebo controlled study. Recombinant TNFR:Fc (etanercept) was used in the study and was administered twice weekly at a flat dose of 25 mg injected subcutaneously. The drug was well tolerated in all patients and the etanercept induced a significant improvement as compared with the placebo group in Psoriatic Arthritis response.

MECHANISM OF ACTION - TNF alpha antagonists.

USE - The TNF receptor is used in the treatment of disorders characterized by abnormal or excessive TNF alpha levels. Bacterial, **viral** or protozoal infections and resulting complications, cardiovascular disorders, chronic pain conditions, disorders of the endocrine system, genitourinary system disorders, various hematological and oncologic disorders, lymphoproliferative disorders, hereditary conditions such as Gaucher's disease, Huntington's disease, linear Immunoglobulin A disease and muscular dystrophy, head and spinal cord injuries, liver disorders, hearing loss disorders, non-arthritic medical conditions of the bones and joints, pulmonary disorders, rheumatic disorders, amyloidosis, disorders of the skin and mucous membranes, transplant disorders, ocular disorders, disorders of the female reproductive system and obesity can be treated and/or prevented.

TNFR:Fc induces an improvement over baseline in an indicator which is psoriasis area and severity index (PASI) or target lesion assessment score.

Dwg.0/0

L178 ANSWER 12 OF 30 MEDLINE
ACCESSION NUMBER: 2000280153 MEDLINE
DOCUMENT NUMBER: 20280153 PubMed ID: 10818004
TITLE: Impaired prion replication in spleens of mice lacking functional follicular dendritic cells.
AUTHOR: Montrasio F; Frigg R; Glatzel M; Klein M A; Mackay F; Aguzzi A; Weissmann C
CORPORATE SOURCE: Institute of Neuropathology, Department of Pathology,

University of Zurich, Schmelzbergstrasse 12, CH-8091 Zurich, Switzerland.
SOURCE: SCIENCE, (2000 May 19) 288 (5469) 1257-9.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000606
Last Updated on STN: 20000606
Entered Medline: 20000525

AB In scrapie-infected mice, prions are found associated with splenic but not circulating B and T lymphocytes and in the stroma, which contains follicular dendritic cells (FDCs). Formation and maintenance of mature FDCs require the presence of B cells expressing membrane-bound **lymphotoxin**-alpha/**beta**. Treatment of mice with **soluble lymphotoxin-beta receptor** results in the disappearance of mature FDCs from the spleen. We show that this treatment abolishes splenic prion accumulation and retards neuroinvasion after intraperitoneal scrapie inoculation. These data provide evidence that FDCs are the principal sites for prion replication in the spleen.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Cell Differentiation: GE, genetics
Cell Differentiation: IM, immunology
Dendritic Cells, Follicular: ME, metabolism
*Dendritic Cells, Follicular: PA, pathology
*Dendritic Cells, Follicular: VI, virology
Immunoglobulins: GE, genetics
Lymphotoxin: AI, antagonists & inhibitors
Lymphotoxin: GE, genetics
Lymphotoxin: IM, immunology
Mice
Mice, Inbred C57BL
Mice, SCID
PrPSc Proteins: AD, administration & dosage
*PrPSc Proteins: BI, biosynthesis
Receptors, Tumor Necrosis Factor: AI, antagonists & inhibitors
Receptors, Tumor Necrosis Factor: GE, genetics
Receptors, Tumor Necrosis Factor: IM, immunology
Recombinant Fusion Proteins: AD, administration & dosage
Scrapie: IM, immunology
Scrapie: ME, metabolism
Signal Transduction: GE, genetics
Signal Transduction: IM, immunology
Spleen: IM, immunology
Spleen: ME, metabolism
*Spleen: PA, pathology
*Spleen: VI, virology
Virus Replication: GE, genetics
***Virus Replication: IM, immunology**

L178 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:502493 HCAPLUS
DOCUMENT NUMBER: 133:206273
TITLE: Temporary inactivation of follicular dendritic cells delays neuroinvasion of scrapie
AUTHOR(S): Mabbott, Neil A.; Mackay, Fabienne; Minns, Fiona; Bruce, Moira E.

CORPORATE SOURCE: Neuropathogenesis Unit, Institute for Animal Health, Edinburgh, EH9 3JF, UK
SOURCE: Nature Medicine (New York) (2000), 6(7), 719-720
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors reported that a single treatment with a fusion protein consisting of lymphotoxin .beta. receptor and human Ig (LT.beta.R-Ig), a treatment that interferes with the integrity of follicular dendritic cells (FDCs), before or shortly after peripheral scrapie challenge was sufficient to substantially slow the transmissible spongiform encephalopathies (TSEs).
CT **Fusion proteins (chimeric proteins)**
CT **Immunoglobulins**
CT Dendritic cell
CT Brain, disease
CT Prion diseases
CT Prion diseases
CT **Lymphokine receptors**

L178 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:425461 HCAPLUS
DOCUMENT NUMBER: 131:72734
TITLE: Methods of treating TNF.alpha.-mediated disease using chimeric anti-TNF antibodies
INVENTOR(S): Le, Junming; Vilcek, Jan; Dadonna, Peter; Ghrayeb, John; Knight, David; Seigal, Scott
PATENT ASSIGNEE(S): New York University, USA; Centocor, Inc.
SOURCE: U.S., 88 pp., Cont.-in-part of U.S. Ser. No. 10,406, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5919452	A	19990706	US 1994-192861	19940204
EP 1097945	A2	20010509	EP 2000-204461	19920318
EP 1097945	A3	20011010		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC				
US 5698195	A	19971216	US 1994-324799	19941018
US 6277969	B1	20010821	US 1998-133119	19980812
US 2001027249	A1	20011004	US 2001-756301	20010108
US 2002022720	A1	20020221	US 2001-927703	20010810

PRIORITY APPLN. INFO.:
US 1991-670827 B2 19910318
US 1992-853606 B2 19920318
US 1992-943852 B2 19920911
US 1993-10406 B2 19930129
US 1993-13413 B2 19930202
EP 1992-910625 A3 19920318
US 1994-192093 B2 19940204
US 1994-192102 A2 19940204
US 1994-192861 B2 19940204
US 1994-324799 A2 19941018
US 1995-570674 B3 19951211
US 1998-133119 A3 19980812
US 2001-756398 A1 20010108

AB Treatment of tumor necrosis factor, TNF, mediated pathologies is provided by administering anti-TNF compds., such as anti-TNF antibodies and anti-TNF peptides, which compds. are specific for tumor necrosis factor-.alpha. (TNF.alpha.) or tumor necrosis factor-.beta. (TNF.beta.) and which are useful for in vivo therapy or diagnosis of TNF.alpha.-mediated pathologies and conditions, wherein the anti-TNF compd. is selected from the group consisting of at least one of an Ig variable region, a fragment of a TNF receptor and an anti-TNF peptide, such as a structural analog of a anti-TNF antibody fragment or a TNF receptor fragment. The anti-TNF antibodies, TNF receptors and their fragments are useful for treating bacterial infection, viral infection, parasitic infection, chronic inflammatory diseases, autoimmune diseases, malignancies, and/or neurodegenerative diseases.

CT **Immunoglobulins**
CT Blood vessel, disease
CT **Fusion proteins (chimeric proteins)**
CT Disease, animal
CT Mouse
CT Rodent
CT Thyroid gland, disease
CT Infection
CT Inflammation
CT Nervous system
CT Blood coagulation
CT Transplant and Transplantation
CT **Immunoglobulins**
CT Arthritis
CT Atherosclerosis
CT Autoimmune disease
CT Diabetes mellitus
CT Epitopes
CT Graves' disease
CT Neoplasm
CT Protein sequences
CT Rheumatoid arthritis
CT Sarcoidosis
CT Sepsis
CT cDNA sequences
CT **Lymphotoxin**
CT Tumor necrosis factors
CT **Antibodies**
CT Parasite
CT Intestine, disease
CT **Immunoglobulins**
CT **Antibodies**
CT Tumor necrosis factor receptors
CT Proteins, specific or class
CT Proteins, specific or class
CT Connective tissue
CT Lupus erythematosus
CT Intestine, disease
CT Infection

REFERENCE COUNT: 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L178 ANSWER 15 OF 30 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-120787 [10] WPIDS
DOC. NO. NON-CPI: N1999-088120
DOC. NO. CPI: C1999-035386
TITLE: New ligand for herpes **virus** entry mediator -

used to develop products for treating e.g. autoimmune disease, lymphomas, leukaemias, **infections**, immunosuppression or AIDS.

DERWENT CLASS: B04 D16 S03
INVENTOR(S): WARE, C F; WARE, C E
PATENT ASSIGNEE(S): (LJOL-N) LA JOLLA INST ALLERGY & IMMUNOLOGY
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9902563	A1	19990121	(199910)*	EN	60
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9882882	A	19990208	(199924)		
EP 1003782	A1	20000531	(200031)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 6140467	A	20001031	(200057)		
CN 1268953	A	20001004	(200067)		
JP 2001509373	W	20010724	(200147)		62
KR 2001021579	A	20010315	(200159)		
AU 741419	B	20011129	(200206)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9902563	A1		WO 1998-US13897	19980707
AU 9882882	A		AU 1998-82882	19980707
EP 1003782	A1		EP 1998-933153	19980707
			WO 1998-US13897	19980707
US 6140467	A	Provisional	US 1997-51964P	19970707
			US 1997-898234	19970730
CN 1268953	A		CN 1998-808663	19980707
JP 2001509373	W		WO 1998-US13897	19980707
			JP 2000-502082	19980707
KR 2001021579	A		KR 2000-700137	20000107
AU 741419	B		AU 1998-82882	19980707

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9882882	A	Based on	WO 9902563
EP 1003782	A1	Based on	WO 9902563
JP 2001509373	W	Based on	WO 9902563
AU 741419	B	Previous Publ.	AU 9882882
		Based on	WO 9902563

PRIORITY APPLN. INFO: US 1997-898234 19970730; US 1997-51964P 19970707

AB WO 9902563 A UPAB: 19990310
The following are claimed: (1) a purified polypeptide characterised by: (a) having a molecular weight of 30 kDa as determined by SDS-PAGE; (b) a pI of about 7 to 8.5; (c) binding to the herpes **virus** entry mediator (HVEM) polypeptide; and (d) binding to the **lymphotoxin**

beta receptor (**LT beta** R) polypeptide; (2) an isolated nucleic acid sequence which encodes a polypeptide as in (A); (3) an expression vector containing a nucleic acid sequence as in (2); (4) a host cell containing a expression vector as in (3); (5) an **antibody** that binds to a polypeptide as in (1); (6) identifying a compound which affects an HVEM-binding agent-mediated cellular response comprising: (a) incubating the compound with an HVEM polypeptide or a cell expressing an HVEM polypeptide, and an HVEM-binding agent, to allow the components to interact; and (b) determining the effect of the compound on the HVEM-binding agent-mediated cellular response; (7) identifying a compound which affects an **LT beta** R-p300-mediated cellular response, comprising: (a) incubating the compound with an **LT beta** R polypeptide or a cell expressing an **LT beta** R polypeptide, and with p30, to allow the components to interact; and (b) determining the effect of the compound on the **LT beta** R-p30-mediated cellular response; (8) modulating an HVEM-mediated cellular response, comprising contacting a cell expressing HVEM with an HVEM binding agent or a p30 binding agent; (9) modulating an HVEM-mediated cellular response comprising contacting a cell expressing the HVEM with an HVEM binding agent or an LT alpha binding agent; (10) modulating an **LT beta** R-mediated cellular response comprising contacting a cell expressing **LT beta** R with an **LT beta** R binding agent or a p30 binding agent, and (11) **inhibiting** herpes simplex **virus** (HSV) infection of a cell, comprising contacting a cell susceptible to HSV infection with a HVEM binding agent, to **inhibit** HSV infection.

USE - The novel 30 kDa polypeptide ligand, designated p30, can bind to HVEM and **LT beta** . The products can be used for detection, diagnosis and screening assays. **Inhibitors** of p30 or LT alpha interactions with HVEM, or p30 interactions with **LT beta** R, could be used to modulate diseases where unwanted lymphocytes proliferation occurs, including T and B lymphomas or leukaemias, or in autoimmune diseases such as rheumatoid arthritis, insulin-dependent diabetes mellitus, multiple sclerosis, systemic lupus erythematosus or myasthenia gravis. They can also be used to **inhibit** herpes **virus** infection by **blocking** the ability of herpes **virus** to enter a cellular target. Compounds which stimulate lymphocyte activation can be used for stimulating immune responses in subjects with infectious diseases, or in which the subject is immunosuppressed as, e.g. in patients undergoing chemotherapy or radiation therapy for cancer or in patients with AIDS.

Dwg.0/7

L178 ANSWER 16 OF 30 MEDLINE

ACCESSION NUMBER: 2000048155 MEDLINE
DOCUMENT NUMBER: 20048155 PubMed ID: 10581078
TITLE: Reversal of **virus**-induced systemic shock and respiratory failure by blockade of the lymphotoxin pathway.
AUTHOR: Puglielli M T; Browning J L; Brewer A W; Schreiber R D; Shieh W J; Altman J D; Oldstone M B; Zaki S R; Ahmed R
CORPORATE SOURCE: Emory Vaccine Center and Department of Microbiology and Immunology, Emory University School of Medicine, Atlanta, Georgia 30322, USA.
CONTRACT NUMBER: AI09866 (NIAID)
AI30048 (NIAID)
NS21496 (NINDS)
SOURCE: NATURE MEDICINE, (1999 Dec) 5 (12) 1370-4.
Journal code: 9502015. ISSN: 1078-8956.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991229

AB At present, little is known about the pathogenesis of acute **virus** -induced shock and pulmonary failure. A chief impediment in understanding the underlying disease mechanisms and developing treatment strategies has been the lack of a suitable animal model. This study describes a mouse model of **virus**-induced systemic shock and respiratory distress, and shows that **blockade** of the **lymphotoxin beta receptor** pathway reverses the disease.

CT Check Tags: Animal; Female; Human; Male; Support, U.S. Gov't, P.H.S.
Antibodies, Monoclonal: PD, pharmacology
Disease Models, Animal
Lymphocytic Choriomeningitis: IM, immunology
Lymphocytic Choriomeningitis: PA, pathology
Lymphocytic Choriomeningitis: TH, therapy
Mice
Mice, Inbred NZB
***Receptors, Tumor Necrosis Factor: AI, antagonists & inhibitors**
Respiratory Insufficiency: IM, immunology
Respiratory Insufficiency: PA, pathology
*Respiratory Insufficiency: TH, therapy
Shock, Septic: IM, immunology
Shock, Septic: PA, pathology
*Shock, Septic: TH, therapy
Signal Transduction
Time Factors

L178 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:438429 HCAPLUS
DOCUMENT NUMBER: 131:256111
TITLE: Lymphotoxin-.beta.-deficient mice show defective antiviral immunity
AUTHOR(S): Berger, Dietmar P.; Naniche, Denise; Crowley, Mary T.; Koni, Pandelakis A.; Flavell, Richard A.; Oldstone, Michael B. A.
CORPORATE SOURCE: Department of Neuropharmacology, Division of Virology, IMM-6, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Virology (1999), 260(1), 136-147
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lymphotoxin .beta. (LT.beta.), a member of the tumor necrosis factor family, plays an important role in lymphoid organogenesis. To det. whether LT.beta. is involved in cellular immunity, the authors investigated the antiviral immune response of LT.beta.-deficient (LT.beta. -/-) mice to lymphocytic choriomeningitis virus (LCMV). Cytotoxic T lymphocyte (CTL) responses to LCMV were severely diminished, leading to viral persistence in brain and kidney. However, major functions of LT.beta.-deficient T lymphocytes and dendritic cells were intact. Reconstitution of irradiated LT.beta. +/+ mice with LT.beta. -/- bone marrow induced a disorganized splenic structure, accompanied by impairment of the LCMV-specific CTL response. These data indicate that the absence of LT.beta. does not affect the intrinsic function of T lymphocytes or of dendritic cells but that the structural integrity of the spleen is

strongly assocd. with generation of antiviral immunity. (c) 1999 Academic Press.
CT **Immunity**
CT T cell (lymphocyte)
CT Mouse
CT Spleen
CT Lymphocytic choriomeningitis virus
CT **Infection**
CT **Lymphotoxin**
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L178 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 1998:268386 HCAPLUS
DOCUMENT NUMBER: 129:3859
TITLE: Soluble lymphotoxin-beta receptors, anti-lymphotoxin receptor antibodies, and anti-lymphotoxin ligand antibodies as therapeutic agents for the treatment of immunological diseases
INVENTOR(S): Browning, Jeffrey; Hochman, Paula Susan; Rennert, Paul D.; Mackay, Fabienne
PATENT ASSIGNEE(S): Biogen, Inc., USA; Browning, Jeffrey; Hochman, Paula Susan; Rennert, Paul D.; Mackay, Fabienne
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9817313	A2	19980430	WO 1997-US19436	19971024
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9850896	A1	19980515	AU 1998-50896	19971024
AU 726357	B2	20001102		
BR 9712670	A	19991019	BR 1997-12670	19971024
EP 954333	A2	19991110	EP 1997-913798	19971024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1237910	A	19991208	CN 1997-199906	19971024
JP 2001502697	T2	20010227	JP 1998-519688	19971024
NO 9901926	A	19990625	NO 1999-1926	19990422

PRIORITY APPLN. INFO.: US 1996-29060P P 19961025
WO 1997-US19436 W 19971024

AB Compns. and methods comprising "lymphotoxin-.beta. receptor blocking agents" which block lymphotoxin-.beta. receptor signalling and are useful for altering immunol. diseases, and particularly antibody mediated immune responses. The lymphotoxin-.beta. receptor blocking agents are monoclonal antibodies, sol. lymphotoxin-.beta. receptor, anti-lymphotoxin ligand antibodies, or fusion protein of sol. lymphotoxin-.beta. receptor and Ig Fc domain. The immunol. disease is e.g. AIDS, HIV infection, graft rejection, etc. Antiviral agent, anti-AIDS agent, or anti-CD40L and other

carrier or adjuvant are also included in the remedy.
CT Glycoproteins, specific or class
CT **Immunoglobulins**
CT Immunostimulants
CT Dendritic cell
CT Immunity
CT **Lymphotoxin**
CT Ligands
CT **Antibodies**
CT AIDS (disease)
CT **Antiviral agents**
CT B cell (lymphocyte)
CT Carriers
CT Human immunodeficiency **virus**
CT Mammal (Mammalia)
CT Protein sequences
CT Transplant rejection
CT **Antibodies**
CT **Lymphokine receptors**

L178 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
ACCESSION NUMBER: 1997:205227 HCAPLUS
DOCUMENT NUMBER: 126:198559
TITLE: Soluble lymphotoxin-.beta. receptors and anti-lymphotoxin receptor and ligand antibodies, as therapeutic agents for the treatment of immunological disease
INVENTOR(S): Browning, Jeffrey L.; Benjamin, Christopher D.; Hochman, Paula S.
PATENT ASSIGNEE(S): Biogen, Inc., USA; Browning, Jeffrey L.; Benjamin, Christopher D.; Hochman, Paula S.
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9703687	A1	19970206	WO 1996-US12010	19960719
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
US 5925351	A	19990720	US 1995-505606	19950721
AU 9665912	A1	19970218	AU 1996-65912	19960719
AU 715407	B2	20000203		
EP 840616	A1	19980513	EP 1996-925393	19960719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1195294	A	19981007	CN 1996-196770	19960719
BR 9609716	A	19990706	BR 1996-9716	19960719
JP 11510488	T2	19990914	JP 1996-506919	19960719
NO 9800172	A	19980323	NO 1998-172	19980114
FI 9800122	A	19980319	FI 1998-122	19980120
US 6403087	B1	20020611	US 1998-166	19980608

PRIORITY APPLN. INFO.: US 1995-505606 A 19950721

WO 1996-US12010 W 19960719

AB This invention relates to compns. and methods comprising "lymphotoxin-.beta. receptor blocking agents", which block lymphotoxin-.beta. receptor signalling. Lymphotoxin-.beta. receptor blocking agents are useful for treating lymphocyte-mediated immunol. diseases, and more particularly, for inhibiting Th1 cell-mediated immune responses, e.g. delayed type hypersensitivity, contact hypersensitivity, tuberculin-type hypersensitivity, granulomatous, organ transplant rejection, and others. This invention also relates to the use of antibodies directed against either the lymphotoxin-.beta. receptor or its ligand, surface lymphotoxin, that act as lymphotoxin-.beta. receptor blocking agents. A novel screening method for selecting sol. receptors, antibodies and other agents that block LT-.beta. receptor signalling is provided.

CT **Immunoglobulins**
CT Antitumor agents
CT Dermatitis
CT Allergy
CT Immunity
CT Transplant and Transplantation
CT T cell (lymphocyte)
CT Tuberculin
CT Intestine, disease
CT Diabetes mellitus
CT **Antibodies**
CT Transplant and Transplantation
CT Tumor necrosis factor receptors
CT **Fusion proteins (chimeric proteins)**
CT Autoimmune disease
CT Granulomatous disease
CT Multiple sclerosis
CT Protein sequences
CT Psoriasis
CT **Antibodies**
CT Eye, disease
CT Eye, disease
CT **Lymphokine receptors**

L178 ANSWER 20 OF 30 MEDLINE
ACCESSION NUMBER: 97461446 MEDLINE
DOCUMENT NUMBER: 97461446 PubMed ID: 9317127
TITLE: Characterization of lymphotoxin-alpha beta complexes on the surface of mouse lymphocytes.
AUTHOR: Browning J L; Sizing I D; Lawton P; Bourdon P R; Rennert P D; Majeau G R; Ambrose C M; Hession C; Miatkowski K; Griffiths D A; Ngam-ek A; Meier W; Benjamin C D; Hochman P S
CORPORATE SOURCE: Department of Immunology, Biogen, Cambridge, MA 02142, USA.. Jeff_Browning@biogen.com
SOURCE: JOURNAL OF IMMUNOLOGY, (1997 Oct 1) 159 (7) 3288-98. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971105
Last Updated on STN: 19971105
Entered Medline: 19971021

AB The lymphotoxin-alpha beta complex (LT alpha beta) is found on the surface

of activated lymphocytes and binds to a specific receptor called the LT beta receptor (LT beta R). In the mouse, signaling through this pathway is important for lymph node development and splenic organization, yet the biochemical properties of murine LT alpha and LT beta are essentially unknown. Here we have used **soluble** receptor-Ig forms of **LT beta R** and TNF-R55 and mAbs specific for murine LT alpha, LT beta, and LT beta R to characterize the appearance of surface LT alpha beta complexes and LT beta R on several common murine cell lines. Cells that bound **LT beta R** also bound **anti**-LT alpha and anti-LT beta mAbs in a FACS analysis. The ability of these reagents to discriminate between surface TNF and LT was verified by analysis of surface TNF-positive, LPS-activated murine RAW 264.7 monocytic cells. Primary mouse leukocytes from spleen, thymus, lymph node, and peritoneum were activated in vitro, and CD4+ and CD8+ T cells as well as B cells expressed surface LT ligand but not the LT beta R. Conversely, elicited peritoneal monocytes/macrophages were surface LT negative yet LT beta R positive. This study shows that on mononuclear cells, surface LT complexes and receptor are expressed similarly in mice and man, and the tools described herein form the foundation for study of the functional roles of the LT system in the mouse.

CT Check Tags: Animal; Comparative Study; Human
Antibodies, Monoclonal: CH, chemistry
Antibody Specificity
B-Lymphocytes: CH, chemistry
Cell Line
Flow Cytometry
Hybridomas
Immunoglobulins: GE, genetics
Immunoglobulins: ME, metabolism
*Lymphocytes: CH, chemistry
Lymphocytes: IM, immunology
*Lymphocytes: ME, metabolism
Lymphoma, T-Cell
***Lymphotoxin: CH, chemistry**
Lymphotoxin: IM, immunology
Macrophages
*Membrane Proteins: CH, chemistry
Membrane Proteins: IM, immunology
Mice
Rats
Receptors, Tumor Necrosis Factor: GE, genetics
Receptors, Tumor Necrosis Factor: ME, metabolism
Recombinant Fusion Proteins: ME, metabolism
Solubility
Species Specificity
T-Lymphocytes: CH, chemistry
Tumor Cells, Cultured
*Tumor Necrosis Factor: CH, chemistry
Tumor Necrosis Factor: IM, immunology
Tumor Necrosis Factor: ME, metabolism

L178 ANSWER 21 OF 30 MEDLINE
ACCESSION NUMBER: 1998079319 MEDLINE
DOCUMENT NUMBER: 98079319 PubMed ID: 9418124
TITLE: Selective disruption of lymphotoxin ligands reveals a novel set of mucosal lymph nodes and unique effects on lymph node cellular organization.
AUTHOR: Rennert P D; Browning J L; Hochman P S
CORPORATE SOURCE: Department of Immunology/Inflammation, Biogen Inc., Cambridge, MA 02142, USA.

SOURCE: INTERNATIONAL IMMUNOLOGY, (1997 Nov) 9 (11) 1627-39.
Journal code: 8916182. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980306
Last Updated on STN: 19980306
Entered Medline: 19980220

AB Lymphotoxin (LT) provides a critical signal for the genesis of lymph nodes (LN) in mice. Here we show that mice treated in utero with LT beta-R-Ig, which binds to the membrane LT alpha 1 beta 2 heterotrimer, lacked most LN, yet retained a set of mucosal surface draining LN. Since mice genetically deficient in LT alpha lack all LN, including the mucosal set, we hypothesize that a novel LT alpha-dependent pathway controls their genesis. This novel set of mucosal LN cannot be discriminated on the basis of addressin expression. The discovery of LN in mice treated with **LT beta-R-Ig fusion protein** in utero allowed us to compare the roles of membrane LT alpha beta or soluble LT alpha/tumor necrosis factor (TNF) in the development of cellular organization in LN and spleen. Our results indicate that both membrane LT alpha beta and soluble LT alpha/TNF mediate T-B cell segregation and the organization of B cell follicles in spleen and LN. Interestingly, while antagonism of membrane LT alpha beta or soluble LT alpha/TNF prevented germinal center (GC) formation in spleen, antagonism of soluble LT alpha/TNF had no effect on LN formation. The data suggest that multiple LT/TNF ligands control B cell follicle organization in the spleen and LN of adult mice, and that the requirements for LT/TNF ligands in GC formation are distinct in the different lymphoid organs.

CT Check Tags: Animal; Female; Human; Male
Antigens, CD: ME, metabolism
Antigens, CD: PH, physiology
Antigens, CD58: ME, metabolism
Antigens, CD58: PH, physiology
Antigens, Surface: BI, biosynthesis
B-Lymphocytes: CY, cytology
Down-Regulation
Ligands
Lymph Nodes: CY, cytology
*Lymph Nodes: EM, embryology
Lymph Nodes: ME, metabolism
Lymphotoxin: AI, antagonists & inhibitors
Lymphotoxin: ME, metabolism
*Lymphotoxin: PH, physiology
Membrane Proteins: ME, metabolism
Membrane Proteins: PH, physiology
Mice
Mice, Inbred BALB C
Mucous Membrane: EM, embryology
Pregnancy
Receptors, Tumor Necrosis Factor: ME, metabolism
Receptors, Tumor Necrosis Factor: PH, physiology
T-Lymphocytes: CY, cytology
Tumor Necrosis Factor: ME, metabolism
*Tumor Necrosis Factor: PH, physiology

L178 ANSWER 22 OF 30 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 97438922 MEDLINE
DOCUMENT NUMBER: 97438922 PubMed ID: 9293389

TITLE: Adenovirus-mediated blockade of **lymphotoxin-beta** inhibits the induction of contact sensitivity in mice.
AUTHOR: Trueb R M; Brown G R; Dougherty I; Valdez-Silva M; Cruz P D Jr
CORPORATE SOURCE: Department of Dermatology, University of Zurich.
CONTRACT NUMBER: 1K1-1DKO2304 (NIDDK)
5PO1-DK42582 (NIDDK)
R29-AI31649-04 (NIAID)
+
SOURCE: EXPERIMENTAL DERMATOLOGY, (1997 Aug) 6 (4) 175-80.
Journal code: 9301549. ISSN: 0906-6705.
PUB. COUNTRY: Denmark
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971105
Last Updated on STN: 19971105
Entered Medline: 19971023

AB **Lymphotoxin-beta** is a newly recognized member of the tumor necrosis factor ligand family. Recent studies have suggested a role for this cytokine in delayed-type hypersensitivity responses. To determine whether **lymphotoxin-beta** contributes to the development of contact sensitivity, we utilized an inhibitor protein that can effectively **block** binding of **lymphotoxin-beta** to its **receptor**. An adenoviral vector was created that encodes for a **lymphotoxin-beta** inhibitor protein consisting of the extracellular domain of the **lymphotoxin-beta** receptor fused to IgG heavy chain. Intravenous injection of the recombinant virus into BALB/c mice yielded plasma levels of inhibitor protein > 500 micrograms that persisted for 1 week. Mice treated in this manner were compared with control animals injected with adenovirus encoding beta-galactosidase, with respect to their ability to mount contact sensitivity responses to epicutaneously applied dinitro-fluorobenzene. Mice transduced with the **lymphotoxin-beta** inhibitor prior to the induction of contact sensitivity showed significantly suppressed ear swelling responses. By contrast, mice treated with the **lymphotoxin-beta** inhibitor prior to the elicitation of contact sensitivity showed no change in ear swelling responses in comparison to controls. These findings indicate that **lymphotoxin-beta** plays an important role in the afferent phase of the contact sensitivity response.

CT Check Tags: Animal; Comparative Study; Female; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
***Adenoviridae: GE, genetics**
*Dermatitis, Contact: ET, etiology
*Dermatitis, Contact: PC, prevention & control
Mice
Mice, Inbred BALB C
Mice, Inbred Strains
***Receptors, Tumor Necrosis Factor: AI, antagonists & inhibitors**
Receptors, Tumor Necrosis Factor: PH, physiology
Recombinant Proteins: BL, blood
Recombinant Proteins: PD, pharmacology
Viral Proteins: BL, blood
Viral Proteins: PD, pharmacology

L178 ANSWER 23 OF 30 EMBASE
ACCESSION NUMBER: 96348247 EMBASE

DOCUMENT NUMBER: 1996348247
TITLE: Disrupted splenic architecture, but normal lymph node development in mice expressing a soluble **lymphotoxin**-.**beta**. receptor-IgG1 fusion protein.
AUTHOR: Ettinger R.; Browning J.L.; Michie S.A.; Van Ewijk W.; McDevitt H.O.
CORPORATE SOURCE: Department of Microbiology, Stanford Univ. School of Medicine,Stanford, CA 94305, United States
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1996) 93/23 (13102-13107). ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Early in ontogeny, the secondary lymphoid organs become populated with numerous cells of mesodermal origin which forms both the lymphoid and stromal elements. The critical receptor/ligand interactions necessary for lymphoid organogenesis to occur are for the most part unknown. Although lymphotoxin- .alpha. (LT.alpha.) has been shown to be required for normal lymph node, Peyer's patch, and splenic development, it is unclear if soluble LT.alpha.3, and/or cell-bound **lymphotoxin**-.alpha.. **beta**. (LT.alpha..beta.) mediate these developmental events. Here we report that blocking LT.alpha..**beta**./**lymphotoxin**-. **beta**. receptor (LT.beta.R) interaction in vivo by generating mice which express a soluble LT.beta.R-Fc fusion protein driven by the human cytomegalovirus promoter results in an array of anatomic abnormalities affecting both the spleen and Peyer's patches, but not the lymph nodes. These results demonstrate that surface LT.alpha..beta. ligand plays a critical role in normal lymphoid organ development.
CT Medical Descriptors:
*lymphoid organ
animal cell
animal experiment
animal tissue
conference paper
controlled study
cytomegalovirus
female
lymph node
male
mouse
nonhuman
peyer patch
priority journal
promoter region
spleen
transgenic mouse
Drug Descriptors:
*hybrid protein
***immunoglobulin g1**
***lymphotoxin**
***tumor necrosis factor receptor**

L178 ANSWER 24 OF 30 MEDLINE
ACCESSION NUMBER: 96224067 MEDLINE
DOCUMENT NUMBER: 96224067 PubMed ID: 8621492

TITLE: Preparation and characterization of soluble recombinant heterotrimeric complexes of human **lymphotoxins** alpha and **beta**.
AUTHOR: Browning J L; Miatkowski K; Griffiths D A; Bourdon P R; Hession C; Ambrose C M; Meier W
CORPORATE SOURCE: Department of Protein Engineering, Biogen, Cambridge, Massachusetts 02142, USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Apr 12) 271 (15) 8618-26.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960627
Last Updated on STN: 19960627
Entered Medline: 19960620

AB The lymphotoxin (LT) protein complex is a heteromer of alpha (LT-alpha, also called tumor necrosis factor (TNF)-beta) and beta (LT-beta) chains anchored to the membrane surface by the transmembrane domain of the LT-beta portion. Both proteins belong to the TNF family of ligands and receptors that regulate aspects of the immune and inflammatory systems. The LT complex is found on activated lymphocytes and binds to the **lymphotoxin-beta** receptor, which is generally present on nonlymphoid cells. The signaling function of this receptor-ligand pair is not precisely known but is believed to be involved in the development of the peripheral lymphoid organs. To analyze the properties of this complex, a soluble, biologically active form of the surface complex was desired. The LT-beta molecule was engineered into a secreted form and co-expressed with LT-alpha using baculovirus/insect cell technology. By exploiting receptor affinity columns, the LT-alpha3, LT-alpha2/beta1, and LT-alpha1/beta2 forms were purified. All three molecules were trimers, and their biochemical properties are described. The level of LT-alpha3-like components in the LT-alpha1/beta2 preparation was found to be 0.02% by following the activity of the preparation in a WEHI 164 cytotoxicity assay. LT-alpha3 with an asparagine 50 mutation (D50N) cannot bind the TNF receptors. Heteromeric LT complexes were prepared with this mutant LT-alpha form, allowing a precise delineation of the extent of biological activity mediated by the TNF receptors. A LT-alpha3 based cytotoxic activity was used to show that the LT-alpha1/beta2 form cannot readily scramble into a mixture of forms following various treatments and storage periods. This biochemical characterization of the LT heteromeric ligands and the demonstration of their stability provides a solid foundation for both biological studies and an analysis of the specificity of the LT-bet a and TNF receptors for the various LT forms.

CT Check Tags: Animal; Human
Amino Acid Sequence
Base Sequence
Biological Assay
Chromatography, High Pressure Liquid
Cytotoxins: CH, chemistry
DNA Primers: CH, chemistry
***Lymphotoxin: CH, chemistry**
Macromolecular Systems
*Membrane Proteins: CH, chemistry
Mice
Molecular Sequence Data
Molecular Weight
Nucleopolyhedrovirus

Recombinant Proteins
Solubility
Spodoptera

L178 ANSWER 25 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97038344 EMBASE
DOCUMENT NUMBER: 1997038344
TITLE: Production of prostaglandin E2 and collagenase is inhibited by the recombinant soluble tumour necrosis factor receptor p55-human .gamma.3 fusion protein at concentrations a hundred-fold lower than those decreasing T cell activation.
AUTHOR: Nicod L.P.; Isler P.; Chicheportiche R.; Songeon F.; Dayer J.-M.
CORPORATE SOURCE: Dr. L.P. Nicod, Respiratory Division, University Hospital, 1211 Geneva 14, Switzerland
SOURCE: European Cytokine Network, (1996) 7/4 (757-763).
Refs: 34
ISSN: 1148-5493 CODEN: ECYNEJ
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB TNF.alpha., and **lymphotoxin** .alpha. (TNF-.**beta**.) are pleiotropic cytokines with regulatory functions in inflammatory reactions and T cell activation. Natural TNF inhibitors such as soluble TNF-binding proteins, i.e. TNFsR55 and TNFsR75, are shed from white blood cells and probably other cells. These naturally occurring inhibitors of TNF are shown to be 10 times less effective than the bivalent antagonist of TNF, recombinant soluble TNF receptor p55-human .gamma.3 fusion protein (rsTNFR-p55.gamma.3), in controlling the release of prostaglandin E2 (PGE2) and collagenase by fibroblasts, as well as in controlling T cell proliferation. In order to block the action of rhTNF-.alpha. added to fibroblasts, a fivefold excess of rsTNFR-p55h.gamma.3 was sufficient, but concentrations of a hundred to a thousand times higher were required to obtain a significant inhibition of T cell activation. This concentration appears to be required to block membrane-bound TNF-.alpha. on peripheral blood mononuclear cells as shown by Scatchard analysis. We additionally show that rsTNFR-p55h.gamma.3 at high concentrations also blocks T cell activation by dendritic cells. In conclusion rsTNFR-p55h.gamma.3 has a much higher anti-inflammatory effect than immunosuppressive effect.

CT Medical Descriptors:
*t lymphocyte activation
article
biosynthesis
controlled study
dendritic cell
fibroblast
human
human cell
human tissue
immunosuppressive treatment
leukocyte
lymphocyte proliferation
mononuclear cell
scatchard plot
Drug Descriptors:
*collagenase: EC, endogenous compound
*prostaglandin e2: EC, endogenous compound
***tumor necrosis factor binding protein**

***tumor necrosis factor receptor**
hybrid protein
recombinant tumor necrosis factor alpha

L178 ANSWER 26 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96275259 EMBASE
DOCUMENT NUMBER: 1996275259
TITLE: Adenoviral gene transfer of a **lymphotoxin** . **beta**. inhibitor protein versus gene-targeted lymphotoxin-.alpha. knockout: Effect on delayed-type cutaneous hypersensitivity versus abnormal development of peripheral lymphoid tissues in lymphotoxin-.alpha.-deficient mice.
AUTHOR: Trueb R.M.; Cruz P.D.; Dougherty I.; Brown G.; Van Huffel C.; Valdez-Silva M.; Beutler B.
CORPORATE SOURCE: Department of Dermatology, University Hospital,Zurich, Switzerland
SOURCE: Dermatology, (1996) 193/2 (174). ISSN: 1018-8665 CODEN: DERAEG
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 013 Dermatology and Venereology
LANGUAGE: English
CT Medical Descriptors:
*delayed hypersensitivity: ET, etiology
*gene targeting
*gene transfer
adenovirus
animal experiment
animal model
conference paper
controlled study
intravenous drug administration
lymphocyte migration
lymphoid organ
lymphoid tissue
morphogenesis
mouse
nonhuman
priority journal
time
Drug Descriptors:
***lymphotoxin**
immunoglobulin g
immunoglobulin heavy chain
inhibitor protein

L178 ANSWER 27 OF 30 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1995-123164 [16] WPIDS
CROSS REFERENCE: 1997-099528 [09]; 1997-280298 [25]
DOC. NO. CPI: C1995-056151
TITLE: Treating tumour necrosis factor-alpha related disease - by admin. of new or known reactively terminated oligo peptide cpd., e.g. for treating inflammation or **infection**.
DERWENT CLASS: B04
INVENTOR(S): BLACK, R A; FITZNER, J N; SLEATH, P R
PATENT ASSIGNEE(S): (IMMV) IMMUNEX CORP
COUNTRY COUNT: 56
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9506031	A1	19950302	(199516)*	EN	68
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE					
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KE KG KP KR KZ LK LT LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA UZ VN					
AU 9475694	A	19950321	(199526)		
NO 9600723	A	19960223	(199619)		
EP 715619	A1	19960612	(199628)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
FI 9600803	A	19960422	(199637)		
JP 09503201	W	19970331	(199723)		79
EP 715619	A4	19970319	(199731)		
NZ 271893	A	19971124	(199802)		
AU 9850302	A	19980305	(199820)		
AU 687436	B	19980226	(199821)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9506031	A1		WO 1994-US9343	19940819
AU 9475694	A		AU 1994-75694	19940819
NO 9600723	A		WO 1994-US9343	19940819
			NO 1996-723	19960223
EP 715619	A1		EP 1994-925940	19940819
			WO 1994-US9343	19940819
FI 9600803	A		WO 1994-US9343	19940819
			FI 1996-803	19960222
JP 09503201	W		WO 1994-US9343	19940819
			JP 1995-507668	19940819
EP 715619	A4		EP 1994-925940	
NZ 271893	A		NZ 1994-271893	19940819
			WO 1994-US9343	19940819
AU 9850302	A	Div ex	AU 1994-75694	19940819
			AU 1998-50302	19980106
AU 687436	B		AU 1994-75694	19940819

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9475694	A	Based on	WO 9506031
EP 715619	A1	Based on	WO 9506031
JP 09503201	W	Based on	WO 9506031
NZ 271893	A	Based on	WO 9506031
AU 687436	B	Previous Publ.	AU 9475694
		Based on	WO 9506031

PRIORITY APPLN. INFO: US 1994-183019 19940118; US 1993-110601 19930823

AB WO 9506031 A UPAB: 19970626
Treatment of a disease characterised by over-prodn. or upregulated prodn. of TNF- alpha comprises admin. of a compsn. contg. a reactively terminated oligopeptide cpd. of formula (I) or its salt and a carrier, where (I) is capable of reducing serum TNF- alpha levels by at least 80% when administered at 24 mg/kg. in a murine model of LPS-induced sepsis syndrome. X-(CHR')m-CHR2-CONH-CHR3CO-(A)n-NHY (I);X = hydroxamic acid,

thiol, phosphoryl or carboxy; m, n = 0-2; R1-R3 = H, alkylene-(cycloalkyl), OR4,SR4,NR4R5, halo, opt. substd. 1-8C alkyl, (1-8C) alkylenearyl, opt. protected naturally occurring alpha -aminoacid side-chain or -R6-R7; R6 = 1-8C alkylene; R7 = OR4, SR4, NR4R5 or halogen; R4, R5 = H or opt. substd. 1-8C alkyl; Y = H, opt. substd. 1-8C alkyl, alkylene-(cycloalkyl), -R8-COOR9 or -R10-NR11R12; R8, R10 = 1-8C alkylene; R9 = H or 1-8C alkyl; R11, R12 = H or opt. substd. 1-8C alkyl; A = opt. protected alpha -aminoacid residue (same or different if n = 2). Cpds. (I) and their salts are new where; Y = -B-NH2; B = opt. substd. 1-8C alkylene;

USE - (I) are metalloprotease **inhibitors**, esp. useful as **inhibitors** of TNF- alpha converting enzyme (TACE). They thus prevent cleavage of cell-bound TNF- alpha and reduce TNF- alpha levels in serum and tissues. TNF- alpha -related disorders which maybe treated using (I) include:(I) systemic inflammatory response syndrome, e.g. sepsis syndrome (e.g. Gram positive a negative sepsis, culture negative or fungal sepsis, urosepsis, meningococcaemia orneutropoenic fever), trauma/haemorrhage, burns, ionising radiation exposure, acute pancreatitis or adult respiratory distress syndrome; (2) reperfusion injury, e.g. post pump syndrome and ischaemia-reperfusion injury; (3) cardiovascular disease, e.g. cardiac stun syndrome, myocardial infarction or congestive heart failure; (4) infectious disease, e.g. HIV infection or neuropathy, meningitis, hepatitis, septic arthritis, peritonitis, pneumonia, epiglottitis, E.coli 0157:H7, haemolytic uraemic syndrome/thrombolytic thrombocytopoenic purpura, malaria, dengue haemorrhagic fever, leishmaniasis, leprosy, toxic shock syndrome, streptococcal myositis, gas gangrene, Mycobacterium tuberculosis, M. avium intracellulare, Pneumocystis carinii pneumonia, pelvic inflammatory disease, orchitis/epidydimitis, legionella, Lyme disease, influenzea A, Erpstein-Barr **virus**, **viral**-associated haemaphagocytic syndrome or **viral** encephalitis/aseptic meningitis; (5) obstetrics/gynaecology problems, e.g. premature labour, miscarriage or infertility; (6) inflammatory disease/autoimmunity, e.g. rheumatoid arthritis/seronegative arthropathy, inflammatory bowel disease, systemic lupus erythematosus, iridocyclitis/uveitis/optic neuritis, idiopathic pulmonary fibrosis, systemic vasculitis/Wegener's granulomatosis, sarcoidosis or orchitis/vasectomy **reversal** procedures; (7) allergic/atopic disesae, e.g. astham, allergic rhinitis, eczema, allergic contact dermatitis, allergic conjunctivitis or hypersensitive pneumonitis; (8) malignancy, e.g. ALL, AML, CML, CLL Hodgkin's disease, non-Hodgkin's lymphom,a MM, Kaposi's sarcoma, colorectal carcinoma, nasopharyngeal carcinoma, malignant histiocytosis or paraneoplastic syndrome/hypercalcaemia of malignancy; (9) transplant problems, e.g. organ transplant rejection or graft- versus host disease; (10) cachexia; (11) congential disorders, e.g. cystic fibrosis, familial haemophagocytic lymphohistiocytosis or sickle cell anaemia; (12) dermatological disorders, e.g. psoriasis or alopecia; (13) neurological disorders, e.g. multiple sclerosis or migraine headaches; (14) renal disorders, e.g. nephrotic syndrome, haemodilysis problems or ureaemia; (15) toxicity e.g. in OKT3, anti-CD3, cytokine or radiation therapy, chemotherapy or chronic salicylate; or (16) metabolic/idiopathic disorders, e.g. Wilson's disease, haemachromatosis, alpha -1-antitrypsin deficiency, diabetes, Hashimoto's thyroiditis, osteoporosis, hypothalamic-pituitary-adrenal axis evaluation or prim. biliary cirrhosis. Pharmaceutical compsns. for treating TNF-alpha related disorders, conditions or diseases are claimed, contg. the new cpds. (I) and opt. a protein having TNF- alpha binding activity. Typical such proteins are anti-TNF **antibodies** and soluble TNF receptors.

ADVANTAGE - (I) selectively **inhibit** TACE, without affecting TNF- **beta** (**lymphotoxin**) serum levels.

Dwg.0/0

L178 ANSWER 28 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95216133 EMBASE
DOCUMENT NUMBER: 1995216133
TITLE: Cytokine (IL-8, IL-6, TNF-.alpha.) and soluble TNF receptor-I release from human peripheral blood mononuclear cells after respiratory syncytial virus infection.
AUTHOR: Arnold R.; Konig B.; Galatti H.; Werchau H.; Konig W.
CORPORATE SOURCE: Lehrst.Med.Mikrobiologie/Immunologie, Arbeitsgr. Infektabwehrmechanismen, Ruhr-Universitat Bochum, Universitatsstrasse 150,44780 Bochum, Germany
SOURCE: Immunology, (1995) 85/3 (364-372).
ISSN: 0019-2805 CODEN: IMMUAM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB During the initial phase of respiratory syncytial virus (RSV) infection, when a low virus-cell ratio is most probable, signs of inflammation are detectable in the infected respiratory tissue. Therefore we analysed the release of the proinflammatory cytokines interleukin-6 (IL-6), IL-8, tumour necrosis factor-.alpha. (TNF-.alpha.), and the soluble form of the TNF receptor-I (sTNFR-I), from peripheral blood mononuclear cells (PBMC) after exposure to low infectious RSV doses (multiplicity of infection, MOI, 0.001-1) and incubation times of up to 24 hr. The PBMC secreted IL-8 in a time and virus dose-dependent fashion. As was verified by Northern blot analysis, the increased IL-8 secretion rate was accompanied by an enhanced IL-8 mRNA steady-state level. The infection of the PBMC after 4 hr post-RSV exposure was verified by detection of RSV(SH) genomic RNA and mRNA after reverse transcription and polymerase chain reaction (PCR) amplification. In addition, after 24 hr post-infection we determined the percentage of infected cells by specific immunofluorescence using monoclonal antibodies directed against the F- and G-proteins. After exposure of PBMC to inactivated RSV, we observed only RSV(SH) genomic RNA and a reduced IL-8 release. Thus, even the binding and/or phagocytosis of RSV by PBMC induced an IL-8 synthesis to some extent. Following an incubation time of 24 hr, PBMC exposed to small RSV doses synthesized and released high amounts of IL-6 into the cell supernatant. In contrast, only low amounts of TNF-.alpha. were released from PBMC. In addition to the release of the proinflammatory cytokines, an enhanced level of the sTNFR-I was measured in the cell supernatants at a MOI of 0.1. However, there was no correlation between TNFR-I membrane expression and cell supernatant concentration. Co-culture experiments performed with PBMC and human epithelial cells (A549) revealed that the enhanced IL-8 secretion profile observed in the co-culture was partially dependent on the cytokines TNF-.alpha., IL-1.beta. and TNF-.**beta./lymphotoxin** released by the cells themselves.
CT Medical Descriptors:
***respiratory syncytial pneumovirus**
*virus infection
article
controlled study
epithelium cell
human
human cell
immunofluorescence
mononuclear cell
priority journal

reverse transcription polymerase chain reaction
virus concentration
virus inactivation
Drug Descriptors:
***tumor necrosis factor receptor**
*cytokine: EC, endogenous compound
*interleukin 6: EC, endogenous compound
*interleukin 8: EC, endogenous compound
*messenger rna: EC, endogenous compound
*tumor necrosis factor alpha: EC, endogenous compound
*virus rna: EC, endogenous compound
monoclonal antibody

L178 ANSWER 29 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94315460 EMBASE
DOCUMENT NUMBER: 1994315460
TITLE: Functional activities of receptors for tumor necrosis factor-.alpha. on human vascular endothelial cells.
AUTHOR: Paleolog E.M.; Delasalle S.-A.J.; Buurman W.A.; Feldmann M.
CORPORATE SOURCE: Sunley Division, Kennedy Institute of Rheumatology, 1 Lurgan Ave,London W6 8LW, United Kingdom
SOURCE: Blood, (1994) 84/8 (2578-2590).
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Tumor necrosis factor-.alpha. (TNF-.alpha.) plays a critical role in the control of endothelial cell function and hence in regulating traffic of circulating cells into tissues in vivo. Stimulation of endothelial cells in vitro by TNF- .alpha. increases the surface expression of leukocyte adhesion molecules, enhances cytokine production, and induces tissue factor procoagulant activity. In the present study, we have examined the relative roles of the two cell surface receptors for TNF-.alpha. (p55 and p75) on endothelial cells, using antibodies with both agonistic and antagonistic activities. We report that anti-p55 receptor agonistic antibody Htr-9 induces the expression of tissue factor antigen and the release of interleukin-8 (IL-8) and granulocyte-macrophage colony-stimulating factor (GM-CSF). In contrast, there is very little or no activation of endothelial cell responses by an anti-p75 agonist. TNF-.alpha.- induced expression of tissue factor and adhesion molecules, and release of IL-8 and GM-CSF, are decreased by antibodies with antagonistic activities for either receptor, although the effect of anti-p55 antibodies is markedly greater than that of anti-p75 antibodies. The responses of endothelial cells to **lymphotoxin**/TNF-. **beta**. are significantly decreased by anti-p55 antagonists alone. Our data suggest that endothelial cell responses to TNF-.alpha., such as expression of tissue factor and adhesion molecules for mononuclear cells, which may be important in the pathogenesis of atherosclerosis, are mediated predominantly, but not exclusively, by the p55 TNF receptor.

CT Medical Descriptors:
*receptor binding
article
cell proliferation
concentration response

controlled study
endothelium cell
human
human cell
priority journal
vascular endothelium
Drug Descriptors:
*cytokine receptor
*cell adhesion molecule: EC, endogenous compound
*cytokine: EC, endogenous compound
***receptor antibody: PD, pharmacology**
*receptor protein: EC, endogenous compound
*recombinant tumor necrosis factor alpha: CB, drug combination
*recombinant tumor necrosis factor alpha: PD, pharmacology
*recombinant tumor necrosis factor alpha: DO, drug dose
*thromboplastin: EC, endogenous compound
basic fibroblast growth factor
endothelial leukocyte adhesion molecule 1
granulocyte macrophage colony stimulating factor: EC, endogenous compound
indometacin
intercellular adhesion molecule 1: EC, endogenous compound
interleukin 6: EC, endogenous compound
interleukin 8: EC, endogenous compound
lymphotoxin: PD, pharmacology
lymphotoxin: CB, drug combination
lymphotoxin: DO, drug dose
monoclonal antibody
monoclonal antibody h 398: CB, drug combination
monoclonal antibody h 398: PD, pharmacology
monoclonal antibody htr 9: DO, drug dose
monoclonal antibody htr 9: PD, pharmacology
monoclonal antibody htr 9: CB, drug combination
monoclonal antibody mr2 1: PD, pharmacology
monoclonal antibody mr2 1: CB, drug combination
monoclonal antibody utr 1: CB, drug combination
monoclonal antibody utr 1: PD, pharmacology
protein p 55: EC, endogenous compound
vascular cell adhesion molecule 1: EC, endogenous compound
unclassified drug

L178 ANSWER 30 OF 30 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 89358132 MEDLINE
DOCUMENT NUMBER: 89358132 PubMed ID: 2548953
TITLE: Comparative study on the antiviral activity of tumor necrosis factor (TNF)-alpha, **lymphotoxin**/TNF-**beta**, and IL-1 in WISH cells.
AUTHOR: Ruggiero V; Antonelli G; Gentile M; Conciatori G; Dianzani F
CORPORATE SOURCE: Institute of Virology, La Sapienza University, Rome, Italy.
SOURCE: IMMUNOLOGY LETTERS, (1989 May) 21 (2) 165-9.
Journal code: 7910006. ISSN: 0165-2478.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19891011
AB We find that pretreatment of WISH cells with tumor necrosis factor

(TNF)-alpha, IL-1, and **lymphotoxin**/TNF-**beta** is capable of inducing an antiviral state in these cells, thereby protecting them from vesicular stomatitis virus cytopathic effect. Furthermore, we find that such a treatment causes a major inhibition of the synthesis of VSV proteins, as analyzed by SDS-PAGE. The 2-5A synthetase activity is also increased by treating the cells with doses of cytokines effective in antiviral protection. In this cell system, inclusion of polyclonal antibodies to IFN-beta during cytokine pretreatment abrogates the antiviral state elicited by the above cytokines, while antibodies to IFN-beta 2/IL-6 fail to abolish the cytokine-induced antiviral effects.

CT Check Tags: Comparative Study; Human; Support, Non-U.S. Gov't
2',5'-Oligoadenylate Synthetase: AN, analysis
2',5'-Oligoadenylate Synthetase: ME, metabolism
Cell Line
Cells, Cultured
Electrophoresis, Polyacrylamide Gel
*Interleukin-1: PD, pharmacology
***Lymphotoxin: PD, pharmacology**
*Tumor Necrosis Factor: PD, pharmacology
***Vesicular stomatitis-Indiana virus: DE, drug effects**
Viral Interference
*Viral Proteins: ME, metabolism